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Effectiveness of Cognitive, Exposure, and Skills Group Manualized Treatments in OIF/OEF Female Veterans

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14. ABSTRACT

The purpose of the study was to evaluate and establish the effectiveness of three treatments for PTSD – exposure, cognitive, and skills (assertiveness/relaxation) therapies—provided in a structured group format in a sample of OEF/OIF female Veterans. The results supported the primary aim of the study, where the manualized group treatment protocol significantly lowered PTSD symptoms (decrease of 24 points on the CAPS) after the 16-week treatment, a finding maintained 3 and 6 months after treatment. The effect size of the change was comparable to treatments delivered in an individual format. Additionally, the treatment improved the participant's life functioning, mental and physical as measured by the SF36 and quality of life, as measured by the QOLI. The subset of participants assessed for neurocognitive functioning and compared to a normal sample showed significantly lower IQ, but still in the normal range, and poorer executive functioning, similar to male combat Veterans with PTSD. The study's findings support the application of cognitive, exposure, and skills therapies delivered in small groups of 3 members, add methodologically sound findings to the paucity of group literature, and for the first time, establish a structure for the delivery of exposure treatment in a group.

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INTRODUCTION

The purpose of the study is to evaluate and establish the effectiveness of three behavioral treatments for PTSD--exposure, cognitive, and skills (assertiveness/relaxation) therapies--provided in a group format. The efficacies of both exposure and cognitive therapies have been well established for PTSD when provided individually and superior to other PTSD treatments. However, the robust effects have not been demonstrated when these therapies are provided in a group format. The scope of the study is to conduct this Randomized Controlled Trial examining a 16-week manualized group treatment approach in a sample of OIF/OEF female PTSD Veterans. The intent is to establish the efficacy of the 16-week treatment in three treatment blocks, and in particular exposure therapy, in a group format to inform the clinical application of these treatments for the systematic use in outpatient clinics.

BODY

The research accomplishments of the study correspond to the Statement of Work timeline and milestones.

I. YEAR 1 SUMMARY:

A. Timeline #1 (months 1-6): 1) Obtain approval by the Research and Development Committee at the NMVAHCS and Institutional Review Board at the University of New Mexico; and 2) hire the psychologist and psychology technician and train both in primary assigned duties (psychology technician to conduct assessments and psychologist in group treatment).

1) IRB Approvals: Approval by the NMVAHCS R&D and UNM IRB committees were obtained by June 7, 2008. Review by the DOD IRB was conducted and completed with approval on December 7, 2008.

2a) Staffing: The Psychologist was hired on July 7, 2008. The Psychology Technician was split into two half time positions and each was filled on 6/10/08 and 6/23/08. Additional funding ($68,750) was provided by the DOD to collect pre/post neuropsychological pilot data to assess for the effects of treatment on Traumatic Brain Injury. The funding was to cover two years of a half-time neuropsychology technician position, and testing materials. The Neuropsychology Technician was hired on 1/8/09.

2b) Training: The initial training of the Psychology Technicians was completed in September, 2008, however practice was delayed until DOD IRB approval on December, 2008, which was completed by January 30, 2009. The training of the Neuropsychology Technician was completed February 28, 2009.

It was anticipated the IRB approvals, hiring, and training would be completed in six months, but due to delay in approval by DOD IRB, the study was delayed by 4 months.

B. Timeline #2 (months 6 through end of year 3): Recruit participants, conduct assessments, and run study subjects through both arms of the study. Recruitment began in December, 2008 and has consisted of distribution brochures to clinics throughout the Albuquerque VA Hospital, Albuquerque and Santa Fe Vet centers, and other VA organizations within study approval. Data was continuously entered and stored on secure, password protected VA network computers. At the end of the first year, 7 study subjects were assessed and randomized in groups of three, two groups into the treatment arm. All group sessions were videotape recorded for fidelity checks.

C. Timeline #3 (month 9 through year 3.8): Data to be entered, statistical programs developed, data analysis begun, and completed. Meetings with the statistician have been conducted to set up the data base for data entry. Data entry was begun and was ongoing. Data analysis was ongoing and manuscripts were prepared.

D. Timeline #4 (month 6 through year 4): Presentation of the protocol at the International Society of Traumatic Stress Studies in year 1, preliminary results in year 2 and 3,

and final results in year 4. A workshop on the study structure was presented at ISTSS in November 2008. The study was presented at the VISN18 Research Forum in Phoenix in April, 2009 and at the Kansas City DOD conference in 2009.

E. Timeline #5 (year 3.8 through year 4): Manuscript write-up. This final timeline was not within review.

II. YEAR 2 SUMMARY:

A. Timeline #1 (months 1-6): Complete. Staffing: The first Study Coordinator/Staff Psychologist resigned on 12/4/09, however continued working one day/week to complete a treatment group and train the new Study Coordinator; the new Study Coordinator position was filled on 8/4/09.

B. Timeline #2 (months 6 through end of year 3): Recruit participants, conduct assessments, and run study subjects through both arms of the study.

1. Recruitment: Recruitment was conducted by the PI and study staff (psychologist and assessment technicians) in several forms: a) Ongoing contact with other VA staff within Behavioral Health and Medical clinics at the NMVAHCS, with the staff's invitation/consent; b) Flyers and brochures placed in clinics throughout the hospital at the NMVAHCS, placed into packets for new patients, distributed within local community (e.g., UNM and CNM campuses), and postings on the approved URLs (e.g., VA internet website, UNM HSC Clinical Trials website, Albuquerque's Craigslist website, and local "Alibi" on-line magazine); c) Informational meetings periodically held at the vet centers (e.g., Albuquerque and Santa Fe); d) Advertisements posted in the local newspaper as well as other local veteran's organization groups; e) Lastly, "Dear Patient" form letters mailed to patients from primary care providers/clinicians with information about the study and contact numbers.

2. Assessments: a) Treatment Arm: Five out of 18 subjects in the treatment arm completed post, 3-, and 6-month assessments and the remaining expected to complete follow-up assessments. b) Waitlist Arm: Three out of 6 wait-list participants completed the pre/post wait-list assessments and the remaining expected to complete follow-up assessments. c) Participants Not Randomized: Two participants did not meet criteria for study; one other participant withdrew requesting treatment (randomized to waitlist).

3. Study Participation: a) Treatment Arm: Eight out of 18 enrolled subjects finished the actual treatment portion of the treatment arm and either completed or are in some phase of follow-up. Another eight enrolled subjects were receiving treatment. Two participants voluntarily withdrew from the treatment arm. b) Waitlist Arm: Three out of 7 enrolled subjects completed the waitlist arm. Two enrolled subjects were in the waitlist arm. Two participants voluntarily withdrew from wait-list arm. c) Projected vs Actual Enrollment Numbers: The original timeline projected 18 treatment arm and 18 wait-list arm subjects (total=36) to be enrolled by the end of Year 2, an 18-month recruitment period. However, due to randomization, the adjusted projected numbers were 21 and 15 for the treatment and waitlist arms, respectively. 18 treatment arm subjects were enrolled (86% of goal) and 7 waitlist arm subjects (47% of goal) for an overall enrollment rate of 69%. The deficit was expected to be compensated for in Year 3, as evidenced by the enrollment figures for the last quarter (5 of 6 for 83% rate). The study progressed as expected.

C. Timeline #3 (months 9 through year 3.8): Timeline #3 includes data entry, developing statistical programs, and initial/final data analysis.

1. Data Entry: Data began and was ongoing for initial and follow-up assessments. Fidelity checks were conducted at regular intervals with data checks for accuracy.

2. Statistical Analyses: The PI and Study Coordinator met regularly with the statistician and statistical analyses were ongoing with regular data checks. Final analyses are not under this review.

D. Timeline #4 (months 6 through year 4): Presentation of preliminary and outcome data at conferences and develop manuscripts.

1. Presentations at Conferences: No presentations were conducted during Year 2, however, during Year 2, three abstracts with preliminary results were submitted to the International Society of Traumatic Stress Studies (ISTSS) conference for presentation in November, 2010 in Quebec, Canada.

2. Manuscripts: Final manuscript preparation is not under review in Year 2. Manuscripts on clinic general psychiatric and outcome data in Military Sexual Trauma (MST) females was submitted and rejected; it will be revised and resubmitted to another journal. A second manuscript on specific group outcome data of exposure therapy was submitted and rejected; manuscript will be revised and resubmitted to another journal.

E. Timeline #5 (year 3.8 through year 4): Write manuscript(s) and submit for publication. This final timeline is not within review.

III. YEAR 3 SUMMARY:

A. Timeline #1 (months 1-6): **Completed**. Staffing Updates: The Study Coordinator position was upgraded to account for the additional clinical and administrative responsibilities assigned to the position. The ½ time Assessment Technician position has remained unfilled and a new study psychologist position was created to conduct fidelity/reliability checks on assessments and treatment group sessions, as well as assist with the clinical duties (co-leading exposure group sessions, providing wait-list supportive individual sessions) and with data analysis and managing the data base. The funding of the new psychologist position was taken from the vacant ½ time technician position and the monies budgeted for the consultant at the Boston VA who was originally slated to conduct reliability/fidelity checks.

B. Timeline #2 (months 6 through end of year 3—adjusted to end of year 4.25): Recruit participants, conduct assessments, and run study subjects through both arms of the study.

1. Recruitment: Recruitment was conducted by the PI and study staff (psychologist and assessment technicians) in several forms: a) Ongoing contact with other VA staff within Behavioral Health and Medical clinics at the NMVAHCS, with the staff's invitation/consent; b) Flyers and brochures placed in clinics throughout the hospital at the NMVAHCS, placed into packets for new patients, distributed within local community (e.g., UNM and CNM campuses), and postings on the approved URLs (e.g., VA internet website, UNM HSC Clinical Trials website, Albuquerque's Craigslist website, and local "Alibi" on-line magazine); c) Informational meetings periodically held at the vet centers (e.g., Albuquerque and Santa Fe); d) Advertisements posted in the local newspaper as well as other local veteran's organization groups; e) Lastly, "Dear Patient" form letters mailed to patients from primary care providers/clinicians with information about the study and contact numbers.

2. Assessments: a) Initial Intake Assessments: 26 new initial assessments were conducted. 5 were randomized to the Treatment arm, 10 to the wait list arm, 7 from wait list to treatment, 2 drop outs, and 2 excluded. Treatment Arm Assessments (post, 3-, and 6-month): A total of 30 assessments were conducted with subjects in the treatment arm (*Note:* this number does not reflect each subject, but rather represents duplicate and triplicate for some subjects). b) Waitlist Arm: 12 wait-list participants completed the post wait-list assessment.

3. Study Participation: a) Treatment Arm: Total number of subjects in the treatment arm for Year 3 was 20 (*Note:* this includes carry-over from Year 2, those who completed treatment and all follow-up assessments, and those still active). Four participants voluntarily withdrew from the treatment arm. b) Waitlist Arm: A total of 17 subjects participated in the waitlist arm of the study in Year 3(*Note:* this includes those who completed waitlist, follow-up assessment, and those still active). Two participants voluntarily withdrew from wait-list arm.

4. Projected vs Actual Enrollment Numbers: For the first three years of the study, enrollment was at 80% of the targeted number. The projected number of subjects to be enrolled and completed by end of Year 3, was 60, but is actually 48. It was expected the deficits would be compensated for in later years, however the actual enrollment has averaged 4.8 subjects per quarter versus the expected enrollment of 6 per quarter. At this rate, the study would not complete enrollment by the end of the 4th year and a one-year extension was necessary to obtain the targeted number of subjects (N=72).

C. Timeline #3 (months 9 through year 3.8—adjusted to end of year 5): Timeline #3 includes data entry, developing statistical programs, and initial/final data analysis.

1. Data Entry: Data entry continued for initial and follow-up assessments. Fidelity checks for data entry were regularly conducted for data accuracy.

2. Statistical Analyses: The PI and Study Coordinator continued to meet weekly with the statistician. Statistical programs were written and data analyses began with regular data checks. Final analyses are not under this review.

D. Timeline #4 (months 6 through year 4—adjusted to end of year 5): Presentation of preliminary and outcome data at conferences and develop manuscripts.

1. Presentations at Conferences: Three abstracts with preliminary results were presented (1 paper and 2 posters) in Year 3 at the International Society of Traumatic Stress Studies (ISTSS) conference in November, 2010 in Quebec, Canada. Two additional abstracts were submitted to the upcoming ISTSS conference in November, 2011, in Washington, DC, and are under review.

2. Manuscripts/Grant Submission: Final manuscript preparation is not under review in Year 3, but has begun. Manuscripts from other studies were revised and resubmitted to scientific journals. A grant was submitted in December, 2010 to VA HSR&D extending and further developing the methodology of the present study, but it was not funded. The grant application will be revised and resubmitted in May 2011. A second grant application was submitted to DoD in May 2011, extending the study to male OIF/OEF veterans.

E. Timeline #5 (year 3.8 through year 4): Write manuscript(s) and submit for publication. This final timeline is not within this review period, however manuscript for main outcome results began.

IV. YEAR 4 SUMMARY:

A. Timeline #1 (months 1-6): **Completed**.

B. Timeline #2 (months 6 through end of year 3—adjusted to end of year 5): Recruit participants, conduct assessments, and run study subjects through both arms of the study.

1. Recruitment (No change from year 3 summary)**:** Recruitment was conducted by the PI and study staff (psychologist and assessment technicians) in several forms: a) Ongoing contact with other VA staff within Behavioral Health and Medical clinics at the NMVAHCS, with the staff's invitation/consent; b) Flyers and brochures placed in clinics

throughout the hospital at the NMVAHCS, placed into packets for new patients, distributed within local community (e.g., UNM and CNM campuses), and postings on the approved URLs (e.g., VA internet website, UNM HSC Clinical Trials website, Albuquerque's Craigslist website, and local "Alibi" on-line magazine); c) Informational meetings periodically held at the vet centers (e.g., Albuquerque and Santa Fe); d) Advertisements posted in the local newspaper as well as other local veteran's organization groups; e) Lastly, "Dear Patient" form letters mailed to patients from primary care providers/clinicians with information about the study and contact numbers.

2. Assessments:

a) Initial Intake Assessments: 40 new initial assessments were conducted. 18 were randomized to the Treatment arm, 16 to the wait list arm, 7 from wait list to treatment, 2 drop outs, and 4 excluded.

b) Treatment Arm Assessments (post, 3-, and 6-month): A total of 98 post, 3-, and 6-month assessments were conducted on subjects in the treatment arm (*Note:* this number does not reflect each subject, but rather represents duplicate and triplicate for some subjects).

c) Waitlist Arm Assessments: 25 wait-list participants completed the post wait-list assessment.

3. Study Participation:

a) Treatment Arm: Total number of subjects in the treatment arm for Year 4 was 30 (*Note:* this includes carry-over from Year 3, treatment completers, and active from both Treatment arm and Waitlist to Treatment subjects). Two participants voluntarily withdrew from the treatment arm and two participants were withdrawn.

b) Waitlist Arm: A total of 13 subjects participated in the waitlist arm of the study in Year 4(*Note:* this includes those who completed waitlist, follow-up assessment, and active). Three participants voluntarily withdrew and one participant was withdrawn from wait-list arm.

4. Projected Enrollment Numbers: Initial projections for the study were 36 randomized to treatment and 36 to waitlist arms (n=72) with carryover of 36 from waitlist to treatment for a total of 72 in the treatment arm and 36 in the waitlist arm (N=108). Based on Year 4 calculations and adjustments for excludes/drop outs, 18 more subjects were required (Treatment=9, Waitlist=9) to complete the study. Enrollment will continue until August 2012.

C. Timeline #3 (months 9 through year 3.8—adjusted to be completed at end of year 5): Timeline #3 includes data entry, developing statistical programs, and initial/final data analysis.

1. Data Entry: Data entry continued for initial and follow-up assessments. Fidelity checks for data entry were regularly conducted for data accuracy.

2. Statistical Analyses: The PI and Study Coordinator continued to meet weekly with the statistician. Statistical programs were written and data analyses began with regular data checks. Final analyses were not under this review.

D. Timeline #4 (months 6 through year 4—adjusted to the end of year 5): Presentation of preliminary and outcome data at conferences and develop manuscripts.

1. Presentations at Conferences: One poster containing preliminary results was presented in Year 4 at the International Society of Traumatic Stress Studies (ISTSS) conference in November, 2011 in Baltimore, MD. One workshop was presented in March 2012 at the Institute on Violence, Abuse, and Trauma (IVAT) in Honolulu, HI.

2. Manuscripts/Grant Submission: Final manuscript preparation has begun. Manuscripts from other studies were being revised and resubmitted to scientific journals. Two grants were in preparation for submission to DoD and VA CSR&D in 2012.

V. YEAR 5 SUMMARY: Timeline #5 No Cost Extension (year 4 through year 5):

A. Timeline #1 (months 1-6): **Completed**.

B. Timeline #2 (months 6 through end of year 5): Recruit participants, conduct assessments, and run study subjects through both arms of the study.

1. Recruitment (through 9/1/12—No change from year 3 summary)**:** Recruitment was conducted by the PI and study staff (psychologist and assessment technicians) in several forms: a) Ongoing contact with other VA staff within Behavioral Health and Medical clinics at the NMVAHCS, with the staff's invitation/consent; b) Flyers and brochures placed in clinics throughout the hospital at the NMVAHCS, placed into packets for new patients, distributed within local community (e.g., UNM and CNM campuses), and postings on the approved URLs (e.g., VA internet website, UNM HSC Clinical Trials website, Albuquerque's Craigslist website, and local "Alibi" on-line magazine); c) Informational meetings periodically held at the vet centers (e.g., Albuquerque and Santa Fe); d) Advertisements posted in the local newspaper as well as other local veteran's organization groups; e) Lastly, "Dear Patient" form letters mailed to patients from primary care providers/clinicians with information about the study and contact numbers.

2. Assessments:

a) Initial Intake Assessments: 10 new initial assessments were conducted. 3 were randomized to the Treatment arm, 5 to the wait list arm, 0 from wait list to treatment, 2 drop outs, and 0 excluded.

b) Treatment Arm Assessments (post, 3-, and 6-month): A total of 41 post, 3-, and 6-month assessments were conducted on subjects in the treatment arm (*Note:* this number does not reflect each subject, but rather represents duplicate and triplicate for some subjects).

c) Waitlist Arm Assessments: 6 wait-list participants completed the post wait-list assessment.

3. Study Participation:

a) Treatment Arm: Total number of subjects in the treatment arm for Year 5 was 25 (*Note:* this includes carry-over from Year 4, treatment completers, and active from both Treatment arm and Waitlist to Treatment subjects). 6 participants voluntarily withdrew from the treatment arm.

b) Waitlist Arm: A total of 7 subjects participated in the waitlist arm of the study in Year 5(*Note:* this includes those who completed waitlist, follow-up assessment, and active). One participant voluntarily withdrew.

4. Final Enrollment Numbers: Initial projections for the study were 36 randomized to treatment and 36 to waitlist arms (n=72) with carryover of 36 from waitlist to treatment and oversampling for a total of 72 in the treatment arm and 36 in the waitlist arm (N=108). Final figures resulted in 97 total subjects enrolled, with 86 meeting eligibility requirements; with 44 randomized to the treatment arm, 42 to the Waitlist arm, and of the latter, 25 requesting study treatment.

C. Timeline #3 (months 9 through end of year 5): Timeline #3 includes data entry, developing statistical programs, and initial/final data analysis.

1. Data Entry: Data entry continued for initial and follow-up assessments. Fidelity checks for data entry are regularly conducted for data accuracy.

2. Statistical Analyses: The PI continued meeting weekly with the statistician. Statistical programs continue to be written and data analyses have begun with regular data checks. Final analyses are not under this review.

D. Timeline #4 (months 6 through year 5): Presentation of preliminary and outcome data at conferences and develop manuscripts.

1. Presentations at Conferences: One paper was presented at the American Psychological Association in August, 2012 in Orlando, FL on the neuropsychological findings.

2. Manuscripts/Grant Submission: Final manuscript preparation has begun. Manuscripts from other studies are being revised and resubmitted to scientific journals. Three grants were submitted to DoD (2, one with Dr. C'de Baca as PI)and VA (1) CSR&D in 2013 to further investigate group exposure therapy.
Manuscript writing has begun.

VI. YEAR 6 SUMMARY: 2nd no Cost Extension (year 5 through year 6 end of study):

A. No changes from Year 5. Study remained open for data analyses, professional presentations, and manuscript preparation.

B. Presentation of preliminary and outcome data at conferences and develop manuscripts.

1. Presentations at Conferences: Five papers were presented on study outcomes, two at the American Psychological Association in August, 2013 in Honolulu, HI; two at the International Society for Traumatic Stress Studies, in Philadelphia, PA; and one at the VISN 18 VA Research Forum.

2. Manuscripts/Grant Submission: The final outcome manuscript was written, submitted on 9/13 to the Journal of Consulting and Clinical Psychology, and rejected. Recommendations on modifications are being made (e.g., intention-to-treat analysis on all data, analyzing data with group as the unit of analysis) including re-analysis and re-writing. A manuscript on the neuropsychological differences was submitted, rejected with recommendation for resubmission (x2), and was resubmitted to the Journal of Traumatic Stress. Two other manuscripts are in preparation, one on ethnicity baseline differences and another on dissociative subtypes, and will be submitted for publication. One DoD grant was funded (Dr. C'de Baca as PI and Dr. Castillo as Co-PI) for 1.7 million examining a 10-session exposure in a 3-person group of OEF/OIF male Veterans. Dr. Castillo's DoD Grant is under review.

KEY RESEARCH ACCOMPLISHMENTS

I. YEAR 1:

1) Successful commencement of research project
2) Hiring and Training of Study Staff
3) Collaboration with Boston Consultants
4) Completed IRB approvals
5) Weekly staff meetings
6) Training materials (videotapes, cds) created
7) Ongoing monitoring of patient safety
8) Expansion of project to add neuropsychological component and staff
9) Successful initiation of recruitment and running of subjects
10) Successful interface with statistician for set up of data base

II. YEAR 2:

1) Completed IRB Reapprovals and Amendments
2) Ongoing weekly research staff meetings to monitor study progress

3) Ongoing recruitment and enrollment of study subjects
4) Ongoing monitoring of patient safety in weekly in staff meetings and annually with independent Medical Monitor
5) Ongoing consultation and collaboration with Boston Consultants
6) Hiring/Training of new Study Coordinator
8) Successful interface with statistician for creating statistical programs and conducting preliminary analyses
9) Successful submissions of abstracts to ISTSS conference for presentation of significant positive results based on initial analyses

III. YEAR 3:

1) Completed. IRB Reapprovals and Amendments are current.
2) Weekly research staff meetings to monitor study progress continue.
3) Recruitment and enrollment of study subjects continues.
4) Patient safety is monitored in weekly in staff meetings and annually with independent Medical Monitor—ongoing.
5) Consultation and collaboration with Boston Consultants—ongoing.
6) Hiring/Training of new study psychologist.
8) Weekly meetings with statistician (creating statistical programs and conducting preliminary analyses)—ongoing.
9) Successful presentations of data at ISTSS conference (2010) showing significant positive outcome results in initial analyses.
10) Submission of abstracts to ISTSS conference (2011) on significant positive longitudinal outcome results from treatment--pending. Total submissions to ISTSS = 4 (includes other non-DoD data).
11) Submission of two new Randomized Control Trials extending this study (one grant compares PE to CPT in group format in male OIF/OEF veterans; second compares PE to PCT in group format in female veterans).

IV. YEAR 4:

1) IRB Reapprovals and Amendments are current.
2) Weekly research staff meetings to monitor study progress continue.
3) Recruitment and enrollment of study subjects continues.
4) Patient safety is monitored in weekly in staff meetings and annually with independent Medical Monitor—ongoing.
5) Consultation and collaboration with Boston Consultants—as needed.
7) Weekly meetings with statistician (statistical programming and conducting preliminary analyses)—ongoing.
8) Fidelity and reliability ratings on Initial and Follow Up Assessments, and on group Treatment blocks (cognitive, exposure, skills) have begun. Fifteen percent of all assessments and treatments will be evaluated for reliability and consistency with protocol.
9) Successful presentations of data at ISTSS (2011) and IVAT (2012) conferences showing significant positive outcome results in initial analyses.
10) Submission of abstracts to APA conference (2012) on significant positive longitudinal outcome results from treatment--pending.
11) Preparation of two new Randomized Control Trials extending this study (one grant compares PE to CPT in group format in male OIF/OEF veterans; second compares individual PE to group PE in female veterans).

V. YEAR 5:

1) IRB Reapprovals and Amendments are current.

2) Weekly research staff meetings to monitor study progress continue.
3) Recruitment and enrollment of study subjects continued through 9/1/2012.
4) Patient safety is monitored in weekly in staff meetings and annually with independent Medical Monitor—ongoing.
5) Consultation and collaboration with Boston Consultants—as needed.
7) Weekly meetings with statistician (statistical programming and conducting preliminary analyses)—ongoing.
8) Fidelity and reliability ratings on Initial and Follow Up Assessments, and on group Treatment blocks (cognitive, exposure, skills) have been completed. Fifteen percent of all assessments and treatments were evaluated for reliability and consistency with protocol and data entered, to be analyzed in year 6.
9) Successful presentations of data at APA (2012) conferences showing significant positive outcome results in initial analyses.
10) Submission of abstracts to ISTSS and APA conferences (2013) on final outcome results—significant positive longitudinal outcome results from treatment and on ethnicity composite of study participants.
11) Two new Randomized Control Trials extending this study (one grant compares PE to CPT in group format (C'de Baca, PI, Castillo, Co-PI) in male OIF/OEF veterans; second (submitted to DoD and VA) compares individual PE to group PE in female veterans) have been completed and submitted for review.

V. YEAR 6 (final):
1) IRB Reapprovals and Amendments are current.
2) Weekly meetings with statistician.
3) Fidelity and reliability ratings on Initial and Follow Up Assessments, and on group Treatment blocks (cognitive, exposure, skills) have been completed. Fifteen percent of all assessments and treatments were evaluated for reliability and consistency. In CAPS assessments, the intra-class correlation was 0.98 and the Kappa statistic was 0.82 for the SCID. In the groups, the reliability was 99% for Exposure, 94% for Cognitive, and 91% for Skills blocks.
4) We found significant improvement in PTSD with the structured group treatment with blocks of Cognitive, Exposure, and Skills treatments (**Aim 1** in SOW).
5) The results showed all three blocks of treatment improved PTSD, with exposure therapy significantly better than cognitive and skills (**Aim 2** in SOW).
6) We successfully established a safe and effective protocol for group delivery of exposure therapy (**Aim 3** in SOW).
7) Neuropsychological differences in baseline IQ and executive function were found with lower IQ and poorer functioning found in the PTSD sample, similar to male combat Veterans (**Aim 4** in SOW). Preliminary analyses are showing that executive function improves with treatment.
8) Results have been successfully presented at APA ISTSS (2013) professional conferences disseminating significant outcome results.
6) Research will be extended in two new Randomized Control Trials, one funded and the other under review.

REPORTABLE OUTCOMES

I. YEAR 1:
1) Presentations to professional groups, including ISTSS, regional VA research conference (VISN 18 Research Forum), and National DOD research conference.

2) Although no data is yet available for analysis/presentation/write-up, manuscript writing on clinical support data continues with submission to one journal. Manuscript was rejected, revisions are being made, and manuscript will be resubmitted to another journal.

II. YEAR 2:

1) Overall descriptive data analyses. For the current 18 subjects, descriptive data reflects a younger (Mean age=34.6 y.o.), well-educated (mean education > 14 years), ethnically diverse sample (white, non-Hispanic < 17%), with many co-morbidities (Axis I=78%, Axis II=22%).
2) Outcome Results. Preliminary analyses on the small number of subjects (n=8) in the treatment arm of the study has shown a statistically significant 20-point reduction of PTSD symptoms (pre to post treatment) on current CAPS scores (preM=58.3, postM=38.4, p<.03), the main outcome measure. Another measure of functioning (SF36) showed significant improvement on four of the eight scales from pre to post treatment. Reductions were on the physical functioning, role limitations due to emotional problems, energy/fatigue, and emotional well-being (p<.05) scales.
3) Study Events. While a small number of subjects have withdrawn from both treatment and waitlist arms of the study, the reasons identified were personal and not study-related. Testimonials from the patients completing the treatment arm have been generally positive. No serious adverse events have occurred; no increases in risk to patients have occurred. No reportable events have occurred.

III. YEAR 3:

1) Overall descriptive data analyses. Preliminary descriptive data (*n*=46) reflected a young (*M*=36), educated (91% some college), ethnically diverse (43% Hispanic, 24% Native American), highly traumatized (94%>3 trauma types; 90%>10 trauma incidents) sample, with Axis I and II co-morbidities (78% and 22%, respectively) and high total Clinician Administered PTSD Scale (CAPS) scores (*M*=156). 2) Longitudinal Outcome Results. A repeated measures analysis of pre, post, 3-, and 6-month follow-up in subjects completing all phases of treatment (*n*=10) showed significant decreases on the total (*p*=.01; *ES*=1.08), re-experiencing (*p*=.02; *ES*=0.79), and avoidance/numbing (*p*=.03; *ES*=1.1) CAPS PTSD scores (20 point decrease maintained at 6 month follow-up). Three of eight SF36 scales (role limitations due to emotional problems, emotional well-being, and social functioning, *p*<.03) also maintained significance at 6 month follow up. 3) Study Events. One study subject randomized to the waitlist arm was hospitalized for psychiatric admission twice within a 4-week period in the last 4 weeks of the 16 week wait list period. Hospitalization was not deemed study related. Withdrawals of other study subjects were also not deemed study-related. Testimonials from the patients completing the treatment arm continue to be generally positive. No increases in risk to patients have occurred.

IV. YEAR 4 (no new analyses):

1) Overall descriptive data analyses. Preliminary descriptive data (*n*=46) reflected a young (*M*=36), educated (91% some college), ethnically diverse (43% Hispanic, 24% Native American), highly traumatized (94%>3 trauma types; 90%>10 trauma incidents) sample, with Axis I and II co-morbidities (78% and 22%, respectively) and high total Clinician Administered PTSD Scale (CAPS) scores (*M*=156).
2) Longitudinal Outcome Results. A repeated measures analysis of pre, post, 3-, and 6-month follow-up in subjects completing all phases of treatment (*n*=10) showed significant decreases on the total (*p*=.01; *ES*=1.08), re-experiencing (*p*=.02; *ES*=0.79), and avoidance/numbing (*p*=.03; *ES*=1.1) CAPS PTSD scores (20 point decrease maintained at 6 month follow-up). Three of eight SF36 scales (role limitations due to emotional problems, emotional well-being, and social functioning, *p*<.03) also maintained significance at 6 month follow up.

3) Study Events. One study subject randomized to the waitlist arm was psychiatrically hospitalized for medication overdose after one month of study participation. Hospitalization was not deemed study related. Determination of withdrawal from study was based on noncompliance in the treatment arm. Testimonials from the study subjects completing the treatment arm continue to be positive. No increases in risk to patients have occurred.

V. YEAR 5 (analyses ongoing):

1) Overall descriptive data analyses. Descriptive data (*n*=86) reflected a young (*M*=36), educated (89% some college), ethnically diverse (40% Hispanic, 17% Native American), highly traumatized (96%>3 trauma types; 92%>10 trauma incidents) sample, with Axis I and II co-morbidities (78% and 22%, respectively) and high total Clinician Administered PTSD Scale (CAPS) scores (*M*=154).

2) Outcome comparison between two arms. An ANOVA comparing pre/post CAPS scores in both study arms (Tx vs. WL) found a significant interaction ($p < .001$) and a significant main effect for the Treatment arm with pre/post CAPS scores decreasing 23 points to below clinic cutoff for the PTSD diagnosis. Secondary analyses are ongoing and will be fully reported in the final report.

3) Longitudinal Outcome Results. A repeated measures analysis of pre, post, 3-, and 6-month follow-up in subjects completing all phases of treatment (*n*=32) showed significant decreases on the total CAPS PTSD scores ($p < .001$; *ES*=1.08), (decreases maintained at 6 month follow-up).

3) Study Events. No events occurred in this period. Testimonials from the study subjects completing the treatment arm have been positive. No increases in risk to patients have occurred.

VI. YEAR 6 (final):

1) Overall descriptive data analyses. Descriptive data (*n*=86) reflected a young (*M*=36), educated (89% some college), ethnically diverse (40% Hispanic, 17% Native American), highly traumatized (96%>3 trauma types; 92%>10 trauma incidents) sample, with Axis I and II co-morbidities (78% and 22%, respectively) and high total Clinician Administered PTSD Scale (CAPS) scores (*M*=154).

2) Outcome comparison between two arms. An ANOVA comparing pre/post CAPS scores in both study arms (Tx vs. WL) found a significant interaction ($p < .001$) and a significant main effect for the Treatment arm with pre/post CAPS scores decreasing 24 points to below clinically significant cutoff for the PTSD diagnosis. The treatment resulted in significant improvement in mental and physical life functioning on the SF36, and in quality of life on the QOLI. All treatment blocks showed PTSD improvement on the PCL, with Exposure significantly better than Cognitive and Skills.

3) Longitudinal Outcome Results. A repeated measures analysis of pre, post, 3-, and 6-month follow-up in subjects completing all phases of treatment (*n*=32) showed significant decreases on the total CAPS PTSD scores ($p < .001$; *ES*=1.08), (decreases maintained at 6 month follow-up).

4) Neuropsychological data showed significantly lower IQ in the PTSD group (still within normal limits) and poorer executive function, similar to male combat Veterans. Preliminary analyses show improved executive function after treatment.

3) Study Events. No events occurred in this period.

CONCLUSION

YEAR 1:

The only problem the study faced was in start up in the wait for DOD IRB review and approval, which delayed commencement of the study. The result was a four-month delay. Despite this delay and once approved, the study began quickly and has experienced no other problems. Data collection and entry was smooth, regular meetings were held within the study staff, with the statistician, and with Boston consultants to assure fidelity of administration of interview instruments.

YEAR 2:

The second year of the study showed a successful follow up to the implementation of the study after the first year. Study enrollment was slightly behind the projected numbers, however enrollment figures suggested the numbers would be made up in year 3. Some study staff have changed, with little break in study function. The main outcome measure for group treatment effectiveness was showing statistically significant with reductions in PTSD symptoms shown with only 8 subjects. Testimonials suggest the treatment was well-tolerated and results show positive effects. The study's positive progress was supported by the independent Medical Monitor. The study staff actively analyzed data and submitted presentation proposals to international conferences.

YEAR 3:

The third year of the study showed continued success in enrollment, randomization, treatment (or waitlist), and follow up assessments. Study enrollment continued to be slightly behind the projected numbers, however enrollment was steady. It was anticipated that a no-cost extension would be submitted 6 months prior to the end of the study in order to collect all the data necessary for a fully powered analysis. Study staffing remained stable and the new staff member helped meet the study goals for completing fidelity and reliability monitoring. The main outcome longitudinal analysis for group treatment effectiveness was statistically significant with reductions in PTSD symptoms maintained 6 months after treatment in 10 subjects. Testimonials suggested the treatment was well-tolerated and results showed positive effects. The study's positive progress was supported by the independent Medical Monitor. The data analysis and conference submission were ongoing and grant funding progressed to replicate and extend positive results.

YEAR 4:

The fourth year of the study continued to show success in enrollment, randomization, treatment (or waitlist), and follow up assessments. Study enrollment continued to be slightly behind the projected numbers, with some slow, but mostly steady periods. The primary problem with study completion was the extended time required (10 month total) for participation in the Treatment Arm (Treatment=4 months, follow up assessments=6 months). It was determined that the last date of enrollment was August 1, 2012. As such, follow up assessments were projected for completion after January 1, 2013 and as late as June, 2013, past the 5th year of the study. In consultation with the grant manager, it was agreed that a 2nd no cost extension would be requested to complete assessments, data analysis and manuscript preparation. The 2nd no-cost extension will be submitted 6 months prior to the end of the study. Study staffing remained stable and fidelity and reliability monitoring began. The main outcome longitudinal analysis for group treatment effectiveness was statistically significant with reductions in PTSD symptoms maintained 6 months after treatment in 21 subjects. Testimonials suggest the treatment was well-tolerated and results showed positive effects. The study's positive progress was supported by the independent Medical Monitor. The data analysis and conference submission was ongoing and grant funding was progressing to replicate and extend positive results.

YEAR 5:

The fifth year of the study showed success in entry, randomization, treatment (or waitlist), and follow up assessments. Enrollment closed on September 1, 2012. Staffing was reduced with the exit of the Study Coordinator in September, 2012 and the two half time Technicians at the end of December, 2012. The treatments were completed in December, 2012 and the last of the follow up assessments were completed the first week of April, one week after the end of the 5th year. A 2nd no cost extension was granted for a full 6th year, however data entry was completed and data analysis and manuscript preparation anticipated to be completed by the end of June 2013. The main outcome longitudinal analysis for group treatment effectiveness was statistically significant with reductions in PTSD symptoms maintained 6 months after treatment. The main outcome manuscript was submitted to the Journal of Consulting and Clinical Psychology. Two additional manuscripts were planned for analyses on ethnic baseline and demographic characteristics and cultural response to exposure therapy. Two oral presentations were accepted by the APA for August, 2013 and one was submitted to ISTSS for November, 2013. Subject testimonials suggest the treatment was well-tolerated and results showed positive effects. The study's positive progress was supported by the independent Medical Monitor. It was anticipated further grant funding will extend the programming of research comparing a stand-alone group exposure model.

YEAR 6 (final):

The six year of the study was successful in completing follow up assessments, data analysis, manuscript writing, and submission. Most successful was study found support for all four aims, including the efficacy of group treatment for PTSD, development of a model to evaluate components of treatment, establishment of a safe/effective group exposure protocol, and improvement of cognitive functioning after PTSD group treatment. Staff were not paid in the final year, however Drs. Castillo and Qualls continued with the statistical analyses for the submission to the Journal of Consulting and Clinical Psychology (JCCP). The manuscript was submitted in September, 2014 and was rejected with encouragement to resubmit. Dr. Paula Schnurr was consulted and provided direction for re-analysis and re-write of the manuscript, which has been ongoing. It is anticipated the revised manuscript will be submitted as a new paper again to JCCP in July, 2014. Two additional manuscripts have been in analysis and preparation, one on ethnic baseline/demographic characteristics and a second on dissociative subtypes of PTSD. A third on cultural response to exposure therapy is being considered. Two other manuscripts on the neuropsychological data are in development, one on baseline differences (resubmitted a 2nd time to Journal of Traumatic Stress) and a second on the impact of PTSD treatment on changes in executive function. The latter is in the data analysis stage. Two oral presentations were conducted, one at the APA in August, 2013 and one at the ISTSS in November, 2013. One presentation was recently accepted at ISTSS in November, 2014. The study was supported by the independent Medical Monitor. It was anticipated further grant funding will extend the programming of research comparing a stand-alone group exposure model.

REFERENCES

Beck, A. T., Ward, C. H., Mendelson, M. Mock, J., & Erbaugh, J. (1961). An inventory for measuring depression. *Archives of General Psychiatry*, *4*, 53-63.

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Klauminzer, G., Charney, D. S., & Keane, T. M. (1990). A clinical rating scale for assessing current and lifetime PTSD: The CAPS-1. *Behavior Therapist*, *18*, 187-188.

Burns, D. D. (1999). *Feeling good: The new mood therapy* (Rev. ed.). New York: Avon Books.

Butcher, J. N. (1989). *Minnesota multiphasic personality inventory-2, user's guide, the Minnesota report: Adult clinical system*. Minneapolis: National Computer Systems.

Castillo, D. T., Nye, E. C., Fallon, S. K., Qualls, C., Sandeen, E. E., & McGlynn, M. A. (n.d.). *Group-based cognitive behavioral interventions for female trauma victims: Effectiveness and self-selection factors*. Manuscript submitted for publication.

Escalona, R., Achilles, G., Waitzkin, H, & Yager, J. (2004). PTSD and somatization in women treated at a VA primary care clinic. *Psychosomatics*, *45*, 291-296.

Foa, E. B., Dancu, C. V., Hembree, E. A., Jaycox, L. H., Meadows, E. A., & Street, G. P. (1999a). The efficacy of exposure therapy, stress inoculation training and their combination in ameliorating PTSD for female victims of assault. *Journal of Consulting and Clinical Psychology*, *67*, 194-200.

Fontana, A. & Rosenheck, R. (1997). *Women under stress: Evaluation of the Women's Stress Disorder Treatment Teams*. West haven, CT: VA Northeast Program Evaluation Center and National Center for PTSD.

Foy, D. W., Glynn, S. M., Schnurr, P. P., Jankowski, M. K., Wattenberg, M. S., Weiss, D. S., Marmar, C. R., & Gusman, F. D. (2000). Group Therapy. In E. B. Foa, T. M. Keane, & M. J. Friedman (Eds.), *Effective treatments for PTSD* (pp. 155-175). New York: The Guildford Press.

Frisch, M. B., Cornell, J., Villanueva, M. & Retzlaff, P. J. (1992). Clinical validation of the Quality of Life Inventory: A measure of life satisfaction for use in treatment planning and outcome assessment. *Psychological Assessment*, *4*, 92-101.

Garrick, J. (2000). Efficacy of PTSD treatment in the VA. *Veterans Health System Journal*, *5*, 15-21.

Gray, M. J., Litz, B. T., Hsu, J. L., & Lombardo, T. W. (2004). Psychometric properties of the life events checklist. *Assessment*, *11*, 330-341.

http://www.oqp.med.va.gov/cpg/cpg.htm. (2003). VA/DoD Clinical Practice Guidelines for the Management of Post Traumatic Stress. Office of Quality and Performance Clinical Practice Guidelines.

Keane, T. M., Fairbank, J. A., Caddell, J. M., & Zimering, R. T. (1989). Implosive (flooding) therapy reduces symptoms of PTSD in Vietnam combat veterans. *Behavior Therapy*, *20*, 245-260.

Keller, M. B., Lavori, P. W., Friedman, B., Nielsen, E., Endicott, J., McDonald-Scott, P., & Andreasen, N. C. (1987). The longitudinal interval follow-up evaluation: A comprehensive method for assessing outcome in prospective longitudinal studies. *Archives of General Psychiatry*, *44*, 540-548.

Kessler, R. C., Sonnega, A., Bromet, E., Hughs, M., & Nelson, C. B. (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of General Psychiatry*, *52*, 1048-1060.

Krakow, B., Hollifield, M., Johnston, L., Koss, M., Schrader, R., Warner, T. D., Tandberg, D., Lauriello, J., McBride, L., Cutchen, L., Cheng, D., Emmons, S., Germain, A., Melendrez, D., Sandoval, D., & Prince, H. (2001). Imagery rehersal therapy for chronic nightmares in sexual assault survivors with posttraumatic stress disorder. *Journal of the American Medical Association*, *286*, 537-545.

Kulka, R. A., Schlenger, W. E., Fairbank, J. A., Hough, R. L., Jordan, B. K., Marmar, C. R., & Weiss, D. S. (1988). Contractual Report of findings from the National Vietnam Veterans Readjustment Study. Volume I: Executive Summary, Description of Findings, and Technical Appendices. Research Triangle Institute, Research Triangle Park, NC.

Lange, A. J. & Jakubowski, P. (1976). *Responsible Assertive Behavior: Cognitive/Behavioral Procedures for Trainers.* Illinois: Research Press.

Millon, T. (1987). *Millon clinical multiaxial inventory II*. Minneapolis: National Computer systems.

Resick, P. A., Jordan, C. G., Girelli, S. A., Hutter, C. K., & Marhoefer-Dvorak, S. (1988). A comparative victim study of behavioral group therapy for sexual assault victims. *Behavior Therapy*, *19*, 385-401.

Resick, P. A. & Schnicke, M. K. (1992). Cognitive processing therapy for sexual assault victims. *Journal of Consulting and Clinical Psychology*, *60*, 748-756.

Resick, P. A. & Schnicke, M. K. (1993). *Cognitive processing therapy for rape victims: A treatment manual*. Newbury Park, CA: Sage.

Rothbaum, B. O., Meadows, E. A., Resick, P., & Foy, D. W. (2000). Cognitive-Behavioral Therapy. In E. B. Foa, T. M. Keane, & M. J. Friedman (Eds.), *Effective treatments for PTSD* (pp. 60-83). New York: The Guildford Press.

Schnurr, P. P., Friedman, M. J., Engle, C. C., Foa, E. B., Shea, M. T., Chow, B. K., Resick, P. A., Thurston, V., Orsillo, S. M., Haug, R., Turner, C., & Bernardy, N. (2007). Cognitive behavioral therapy for posttraumatic stress disorder in women: A randomized controlled trial. *Journal of American Medical Association*, *297*, 820-830.

Schnurr, P. P., Friedman, M. J., Foy, D. W., Shea, M. T., Hsieh, F. Y., Lavori, P. W., et al. (2003). Randomized trial of trauma-focused group therapy for posttraumatic stress disorder. *Archives of General Psychiatry*, *60*, 481-489.

Silver, S. M., Brooks, A., & Obenchain, J. (1995). Treatment of Vietnam war veterans with PTSD: A comparison of eye movement desensitization and reprocessing, biofeedback, and relaxation training. *Journal of Traumatic Stress*, *8*, 337-342.

Wagner, A. W., Wolfe, J., Rotnitsky, A., Proctor, S. P., & Erikson, D. J. (2000). An investigation of the impact of posttraumatic stress disorder on physical health. *Journal of Traumatic Stress*, *13*, 41-55.

Ware, J. E. & Sherbourne, C. D. (1992). The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. *Medical Care*, *30*, 473-483.

Watson, C. G., Tuorila, J. R., Vickers, K. S., Gearhart, L. P., & Mendez, C. M. (1997). The efficacies of three relaxation regiments in the treatment of PTSD in Vietnam War veterans. *Journal of Clinical Psychology*, *53*, 917-923.

Weathers, F. W., Litz, B. T., Herman, D. S., Huska, J. A., & Keane, T. M. (1993, October). *The PTSD checklist (PCL): Reliability, validity, and diagnostic utility*. Paper presented at the 9th Annual Meeting of the International Society for Traumatic Stress Studies, San Antonio, TX.

Yalom, I. (1995). *The Theory and Practice of Group Psychotherapy* (4th ed.). New York: Basic Books.

APPENDICES

APPENDIX A—LIST OF PAID PERSONNEL

1. Study Coordinators: Catherine Hearne, Ph.D., Christine Chee, Ph.D.
2. Study Psychologist: Rachel Freund, Ph.D.
3. Assessment Technicians: Paulette Christopher, Jenny Reinhart, Jenna Keller (Kicklighter), Erica Nason
4. Statistician: Clifford Qualls, Ph.D.
5. Trainer/Consultant: Annemarie Reardon, Ph.D.

APPENDIX B—BIBLIOGRAPHY OF PUBLICATIONS

Year 1 (2008):

1. **Castillo, D. T.**, Keane, T. M., & Montgomery, C. (2008, November). A Manualized Group Protocol of Exposure, Cognitive, and Behavioral Treatments for PTSD. Workshop presented at the International Society for Traumatic Stress Studies, Chicago, IL.
2. **Castillo, D. T.** (2009). Effectiveness of Cognitive, Exposure, and Skills Group Manualized Treatments in OIF/OEF Female Veterans. Abstract for Kansas City DOD Research Conference.

Year 2 (2009): None study-related

Year 3 (2010):

1. Rinehart, J. K., Keller, J., Leiphart, S., **Castillo, D. T**., & Haaland, K. Y. (2010, November). Development of an Emotional Stroop Task for OIF/OEF Female Veterans: Preliminary Findings. Poster presented at the International Society for Traumatic Stress Studies, Montreal, Canada.

Year 4 (2011):

1. **Castillo, D. T.** (2011 February). Group Delivery of Cognitive, Exposure, and Skills Treatments in OIF/OEF Female Veterans: Preliminary Findings from a RCT. VISN 18 Research Forum, Tucson, AZ.
2. **Castillo, D. T**., Chee, C., Nason, E., Keller, J., & Qualls, C. (2011, November). A Randomized Controlled Trial for Group Exposure, Cognitive, and Skills Therapies in Female OEF/OIF Veterans. Poster presented at the International Society for Traumatic Stress Studies, Baltimore, MD.
3. Nason, E., C'de Baca, J., & **Castillo, D. T**. (2011, November). Personality Patterns of Non-Hispanic White, African American, and Hispanic Women Veterans Diagnosed with PTSD. Poster presented at the International Society for Traumatic Stress Studies, Baltimore, MD.
4. **Castillo, D. T.** (2011, August). Group Delivery of Cognitive, Exposure, and Skills Treatments in OIF/OEF Female Veterans: Preliminary Findings. Paper presented at the American Psychological Association conference, Washington, D.C.

Year 5 (2012):

1. **Castillo, D. T.** (2012, March). Expanding Options for Exposure and Cognitive PTSD Therapies: Preliminary Findings from a Group Protocol. Workshop presented at the Institute on Violence and Trauma conference, Honolulu, HI.

Year 6 (2013):

1. **Castillo, D. T.**, Chee, C. L., Nason, E., & Keller, J. (2013, November). Findings from a Randomized Controlled Trial of Group Delivered Evidence-Based PTSD Therapies in OEF/OIF Women Veterans. Paper presented at the International Society for Traumatic Stress Studies Conference, Philadelphia, PA.
2. **Castillo, D. T.**, Chee, C. L., Nason, E., & Keller, J. (2013, August). Efficacy of Group Delivered Evidence-Based PTSD Therapies in Female OIF/OEF Veterans. Paper presented at the American Psychological Association Conference, Honolulu, HI.
3. Nason, E., Keller, J., Chee, C. L., & **Castillo, D. T.** (2013, August). Ethnic Differences in Female OIF/OEF Veterans with PTSD. Paper presented at the American Psychological Association Conference, Honolulu, HI.
4. **Castillo, D. T.** (2013 August). A Randomized Controlled Trial for Efficacy of Group Delivered Evidence-Based Treatments for PTSD in OIF/OEF Women Veterans. VISN 18 Research Forum, Albuquerque, NM.

APPENDIX C—MEETING ABSTRACTS

Year 1 (2008):

1. Castillo, D. T., Keane, T. M., & Montgomery, C. (2008, November). A Manualized Group Protocol of Exposure, Cognitive, and Behavioral Treatments for PTSD. Workshop presented at the International Society for Traumatic Stress Studies, Chicago, IL.

Abstract: The purpose of this workshop is to present a group protocol treatment for PTSD from a recently funded study and will detail how effective therapy interventions—exposure, cognitive, and behavioral—can be provided in structured, small groups. Therapies found most effective for PTSD are exposure and cognitive, with less support for other treatments (Rothbaum, et. al., 2000). Studies have been conducted individually, while most PTSD treatments in VA hospitals are conducted in groups (Garrick, 2000). The literature has shown no difference between specific interventions in groups, including exposure in a group format (Schnurr, et. al., 2003), while support for group exposure was found in a clinical setting (Castillo, 2004). METHODOLOGY: Assessment: pre, post, 3-, and 6-month post treatment; between treatment blocks. Procedure: 72 female OIF/OEF veterans positive for PTSD randomized into a three-person, 16-week treatment group or wait-list control. Blocks: Exposure: trauma and safety nets identified; imaginal exposure. Cognitive: didactic cognitive restructuring, writing of beliefs on safety, trust, power/competence, and esteem/intimacy, distortions examined in session. Behavioral: didactic and videotaped role-play assertiveness training, 4 relaxation techniques. Attendees will gain information on the application of evidence-based treatments for PTSD in a manualized treatment group.

2. Castillo, D. T. (2009). Effectiveness of Cognitive, Exposure, and Skills Group Manualized Treatments in OIF/OEF Female Veterans. Abstract for Kansas City DOD Research Conference.

Abstract: This presentation will provide details from the DOD funded study intended to investigate a group therapy treatment protocol for PTSD in female OIF/OEF veterans. The presentation will consist of a literature review, rationale, and description of the study. The established effective therapy interventions for PTSD, exposure, cognitive, and behavioral, will be examined systematically in small, structured groups of three women. Therapies found most effective for PTSD are exposure and cognitive, with lower effect sizes for other treatments (Rothbaum, et. al., 2000). Most studies have examined the individual administration of these therapies, while most PTSD treatments in VA hospitals are conducted in groups (Garrick, 2000). In general, therapies for PTSD offered in groups have been found equally effective and specifically no differences were found between exposure therapy and present centered therapy in a group format (Schnurr, et. al., 2003). In a clinical setting (Castillo, 2004), support for group exposure was found in small structured groups. METHODOLOGY: The study assessment (SCID I/II, CAPS, LEC, others) will consist of an extensive pre, post, 3-, and 6-month follow up and the PCL will be administered between treatment blocks. After assessment, 72 female OIF/OEF veterans positive for PTSD randomized into a three-person, 16-week treatment group or wait-list/minimal attention control. The 16-weeks of treatment will consist of structured therapy in three blocks: Exposure: trauma and safety nets identified; imaginal exposure. Cognitive: didactic cognitive restructuring, writing of beliefs on safety, trust, power/competence, and esteem/intimacy, distortions examined in session. Behavioral: didactic and videotaped role-play assertiveness training, 4 relaxation techniques. Attendees will gain information on the application of evidence-based treatments for PTSD in a manualized treatment group.

Year 3 (2010):

1. Rinehart, J. K., Keller, J., Leiphart, S., **Castillo, D. T**., & Haaland, K. Y. (2010, November). Development of an Emotional Stroop Task for OIF/OEF Female Veterans: Preliminary Findings. Poster presented at the International Society for Traumatic Stress Studies, Montreal, Canada.
Abstract: PTSD is associated with automatic biases in selective attention. The emotional Stroop task has been used to measure this bias in male combat veterans and female sexual assault victims. No research has investigated female veterans who have PTSD associated with combat and/or sexual trauma. In order to construct a valid Stroop task for this group, neutral, social anxiety, combat, and sexual trauma words were obtained from previous studies (e.g. Foa et al., 1991; McNally et al., 2000) and generated by therapists treating female veterans with PTSD. The therapists rated 90 combat and sexual trauma words for emotional salience, and the ten most salient words in each category were selected for the current task. The emotional salience ratings of female veterans with PTSD and a demographically-matched healthy control group were compared. Preliminary data suggests that neutral words were rated similarly (p = .750), but combat words (t = 3.50, p <.01), sexual trauma words (t = 2.74, p <.05), and social anxiety words (t = 2.16, p =.045) were rated as more emotionally upsetting by the PTSD group. These results support the face validity of this Stroop task to assess attentional biases associated with PTSD due to combat and sexual trauma.

Year 4 (2011):

1. Castillo, D. T. (2011 February). Group Delivery of Cognitive, Exposure, and Skills Treatments in OIF/OEF Female Veterans: Preliminary Findings from a RCT. VISN 18 Research Forum, Tucson, AZ.
Abstract. Group delivery of exposure and cognitive therapies has not demonstrated the comparable robust effects the individual literature has shown in PTSD improvement (Cahill, et. al., 2009). A Randomized Controlled Trial (RCT) examined a 16-week group delivery of exposure, cognitive, and skills treatment blocks in female Iraq/Afghanistan veterans with PTSD. Preliminary descriptive data (n=46) reflected a young (M=36), educated (91% some college), ethnically diverse (43% Hispanic, 24% Native American), highly traumatized (94%>3 trauma types; 90%>10 trauma incidents) sample, with Axis I and II co-morbidities (78% and 22%, respectively) and high total Clinician Administered PTSD Scale (CAPS) scores (M=156). A repeated measures analysis of pre, post, 3-, and 6-month follow-up in subjects completing treatment (n=10) showed significant decreases on the total (p=.01; ES=1.08), re-experiencing (p=.02; ES=0.79), and avoidance/numbing (p=.03; ES=1.1) CAPS scores. Additionally, significant improvement was found on three of eight SF36 scales (role limitations due to emotional problems, emotional well-being, and social functioning, p<.03). Initial comparisons on the PTSD Symptom Checklist (PCL; n=22) between blocks of treatment (cognitive, exposure, skills) showed significant PTSD decreases in the skills group block; data will be analyzed controlling for block order effects. Detailed descriptive data and outcome analyses with implications will be presented.
2. Castillo, D. T., Chee, C., Nason, E., Keller, J., & Qualls, C. (2011, November). A Randomized Controlled Trial for Group Exposure, Cognitive, and Skills Therapies in Female OEF/OIF Veterans. Poster presented at the International Society for Traumatic Stress Studies, Baltimore, MD.
Abstract. Group delivery of exposure and cognitive therapies has not demonstrated the comparable robust effects the individual literature has shown in PTSD improvement (Cahill, et. al., 2009). A Randomized Controlled Trial (RCT) examined a 16-week group delivery of exposure, cognitive, and skills treatment blocks in female Iraq/Afghanistan veterans with PTSD. Preliminary descriptive data (n=46) reflected a young (M=36), educated (91% some college), ethnically diverse (43% Hispanic, 24% Native American), highly traumatized (94%>3 trauma types; 90%>10 trauma incidents) sample, with Axis I and II co-morbidities (78% and 22%, respectively) and high total Clinician Administered PTSD Scale (CAPS) scores (M=156). A

repeated measures analysis of pre, post, 3-, and 6-month follow-up in subjects completing treatment (*n*=10) showed significant decreases on the total (*p*=.01; *ES*=1.08), re-experiencing (*p*=.02; *ES*=0.79), and avoidance/numbing (*p*=.03; *ES*=1.1) CAPS scores. Additionally, significant improvement was found on three of eight SF36 scales (role limitations due to emotional problems, emotional well-being, and social functioning, *p*<.03). Initial comparisons on the PTSD Symptom Checklist (PCL; *n*=22) between blocks of treatment (cognitive, exposure, skills) showed significant PTSD decreases in the skills group block; data will be analyzed controlling for block order effects. Detailed descriptive data and outcome analyses with implications will be presented.

3. Nason, E., C'de Baca, J., & **Castillo, D. T**. (2011, November). Personality Patterns of Non-Hispanic White, African American, and Hispanic Women Veterans Diagnosed with PTSD. Poster presented at the International Society for Traumatic Stress Studies, Baltimore, MD.

Abstract. Prevalence rates in the United States of any Personality Disorder are 9.1% (Lenzenweger, Lane, & Kessler, 2007). Personality Disorders are inflexible patterns of perceiving, reacting, and relating to people and events, impairing the ability to function socially (American Psychiatric Association, 1994). A growing literature indicates personality pathology may be higher in those experiencing trauma and diagnosed with posttraumatic stress disorder (PTSD; Ghafoori & Hierholzer, 2010; Daud, Klinteberg, & Rydelius, 2007; Dunn et al., 2004; Yen et al., 2002). Among traumatic events, rape and combat exposure pose the highest risk for development of PTSD (Kessler et al., 1995; Wolfe et al, 1998; Fontana, Litz, & Rosenheck, 2000). Racial and ethnic differences in personality pathology in this population (women veterans) is less understood (Ghafoori & Hierholzer, 2010). Understanding cultural differences in the expression of symptoms is important to treatment planning. The study population is comprised of 398 women veterans diagnosed with PTSD based on the Clinician Administered PTSD Scale, and who completed the Millon Clinical Multiaxial Inventory-III. Thirty-four percent met criteria for a Cluster A Personality Disorder (PD), 19% for Cluster B PD, and 43% for Cluster C PD. We will examine ethnic differences in Personality Disorders among female veterans in treatment for PTSD.

4. Castillo, D. T., Chee, C., Freund, R, Nason, E., & Keller, J. (2011, August). Group Delivery of Cognitive, Exposure, and Skills Treatments in OIF/OEF Female Veterans: Preliminary Findings. Paper presented at the American Psychological Association conference, Washington, D.C.

Ethnic and Trauma Characteristics in Females with PTSD: Outcomes from a Group Protocol

Diane Castillo, Christine Chee, Rachel Freund, Erica Nason, & Jenna Keller

Statement of Problem. The effectiveness of Evidence-Based Psychotherapies (EBPs) such as exposure and cognitive interventions, is well established for PTSD, however it is important to examine the application of treatment protocols in ethnic minorities with a multiplicity in type and number of traumas when offered in a group format. This randomized control trial with female Iraq/Afghanistan (OIF/OEF) Veterans examines the complexity of trauma history, ethnic background, and response to a 16-week structured group protocol with three blocks of exposure, cognitive, and skills interventions. The sample's ethnicity (42% Hispanic, 24% Native American) and trauma characteristics (70% > 8 trauma types, 69% > 25 trauma incidents, 48% sexual assault, 72% combat) provide an opportunity to examine the impact of these variables on treatment outcome, which will be presented. Preliminary outcome analyses on the overall sample have shown significant reduction of PTSD symptoms (20 point decrease) maintained at 3 and 6 months, which suggest the efficacy and utility in the administration of manualized group EB therapies in treating PTSD. **Introduction** Cognitive and exposure Evidence-Based Psychotherapies (EBP)s for PTSD are most often investigated in an individual format, particularly exposure therapy, while historically PTSD treatments have been offered in unstructured groups in VA outpatient PTSD clinics (Garrick, 2000). However, the research on the group administration of EBPs for PTSD is limited, and the studies available are generally

less rigorous in methodology than the literature on individual delivery (Shea, et al., 2009). Additionally, while higher rates of PTSD have been found in ethnic minority samples and in female Veterans, the literature has yet to investigate the applicability of the EBPs in these populations either in group or individual formats. The few studies that have examined EBPs in a group format typically mix different therapy components (exposure, cognitive, skills) making it difficult to examine the contributions of each intervention and those that have included exposure in group (Schnurr, et al., 2003; Ready, et al., 2008) limit the in-session imaginal exposures to two per patient. Castillo (2004) developed a group program to treat female veterans, separating protocols by groups, which was modified for the present study to examine the effectiveness of group therapy while maximizing adherence to EBP protocols by separating each intervention into treatment blocks. The large ethnic sample and extensive trauma assessment allow examination of these variables on outcome.**Participants.** Demographic data describing ethnicity (17% non-Hispanic White, 42% Hispanic, 27% Native American) and trauma details will be reported on 72 female OIF/OEF Veterans with PTSD. Outcomes for each of three ethnic groups will be reported on 21 participants completing treatment. **Measures.** Descriptive measures included: Structured Clinical Interview for DSMIV, Axis I and II (SCID I/II, Demographics, Life Events Checklist (LEC; 70% > 8 trauma types, 69% > 25 trauma incidents), Military Stress Exposure Questionnaire (MSEQ; 48% sexual assault, 72% combat), Quality of Life Inventory (QOLI), Health Care Utilization, and Medications. Outcome measures included: Clinician Administered PTSD Scale (CAPS), Health Related Quality of Live (SF-36), PTSD Symptom Checklist (PCL), and Health Care Utilization across treatment. **Procedure.** Subjects were randomized by groups of three into one of two arms: a 16-week treatment group or a 16-week minimal attention/wait-list control group. The 16-week treatment group consisted of three blocks: 5 weeks of exposure, 5 weeks of cognitive, and 4 weeks of skills (assertiveness and relaxation training). The first and last sessions did not contain active treatment and block order was controlled. The minimal attention/Wait List (MA/WL) arm consisted of bi-monthly, individual supportive psychotherapy throughout 16 weeks. The PTSD Symptom Checklist (PCL) was administered between blocks and every four weeks in the MA/WL. Assessments were conducted post treatment/WL, and 3 and 6 months after treatment. **Results.** In the initial 72 enrolled participants, the overall demographics were of a young (*M*=37), educated (*M* yrs=14), and ethnically diverse sample (17% non-Hispanic White, 42% Hispanic, 27% Native American,) with multiple traumas. The LEC shows a highly traumatized sample (70% >8 trauma types, 69% >25 trauma incidents). The MSEQ shows few involved in shooting at the enemy, killing of enemy soldiers, civilians, or prisoners (82-97%), however dangerous combat duty ranged from 50% to 74%. Regarding sexual harassment and assault, 97% experienced at least one incident of verbal sexual harassment, 65% experienced at least one incident of physical sexual harassment and as many as 48% reported experiencing rape at least once, with 24% experiencing four or more rapes in the military. The sample shows high co-morbidities (78% Axis I and 22% Axis II) with a high total CAPS *M*=156 (*SD*=35). The outcome results show significant improvement on current PTSD on the CAPS and on three of the eight life functioning scales (SF36), with improvement sustained at 3- and 6-month follow up. A RM-ANOVA with three ethnic groups (non-Hispanic White, Hispanic, Native American) as one factor will be conducted on the Clinician Administered PTSD Scale to compare any differential improvement. A MANCOVA will be conducted will be conducted using trauma types and numbers as a covariant.**Conclusion.** The preliminary results are extremely promising for the group treatment for PTSD in significantly reducing PTSD symptoms and improving social, physical and emotional functioning. This randomized control clinical trial provides the scientific rigor lacking in the group literature and is showing the overall effectiveness of group treatment. Additionally, the design offers an opportunity to evaluate responsivity to treatment by ethnic background and by trauma type/number. The differential contribution of each treatment type--cognitive, exposure, and skills therapies--by separating the treatments into blocks.

Year 5 (2012):

1. Castillo, D. T. (2012, March). Expanding Options for Exposure and Cognitive PTSD Therapies: Preliminary Findings from a Group Protocol. Workshop presented at the Institute on Violence and Trauma conference, Honolulu, HI.

Abstract. This Randomized Controlled Trial (RCT) examined a 16-week group protocol with blocks of exposure, cognitive, and skills treatments in a sample of Iraq and Afghanistan female Veterans with Post Traumatic Stress Disorder (PTSD). A repeated measures ANOVA of pre, post, 3-, and 6-month follow up in the treatment condition showed significant decreases on the Clinician Administered PTSD Scale (CAPS), the main outcome measure for PTSD and on a secondary measure of life functioning (SF36), replicating findings from the individual literature. The group treatment protocol, methods, and results will be discussed.

Objectives: Participants will be able to:

1. Identify two differences in the literature between individual and group delivered evidence-based therapies for PTSD.
2. Describe one essential component of structured group exposure therapy.
3. Identify one significant finding of group delivery of cognitive and exposure evidence-based therapies for PTSD.

Year 6 (2013):

1. Castillo, D. T., Chee, C. L., Nason, E., & Keller, J. (2013, November). Findings from a Randomized Controlled Trial of Group Delivered Evidence-Based PTSD Therapies in OEF/OIF Women Veterans. Paper presented at the International Society for Traumatic Stress Studies Conference, Philadelphia, PA.

Abstract. Exposure and cognitive evidence-based psychotherapies (EBPs) for PTSD are supported in an individual delivery format, with little evidence for superiority in a group (Sloan, et al., 2011). Cognitive therapy components are easily transferred to a group setting, but exposure therapy faces logistic challenges (e.g., repeated in-session imaginal exposure). This randomized controlled trial (RCT) examined a 16-week group treatment with three blocks (cognitive, exposure, skills) and only 3 participants per group versus a minimal attention wait list arm in 86 Afghanistan and Iraq women Veterans. The sample was young (M =36), educated (M=15 yrs), ethnically diverse (42% Hispanic, 17% Native American), and highly traumatized (66%>25 traumas, 69%>8 trauma types; 46% sexual assault). An ANOVA showed a significant (p<.01) pre/post interaction and Repeated Measures ANOVA a significant (p<.001) 23-point CAPS decrease, maintained 6 months after treatment. Full data analysis will be presented including supportive outcome results (SF-36 and QOLI), intent-to-treat analysis, account for intraclass correlation (group as unit of analysis), and PCL comparisons of treatment blocks. This RCT demonstrates the efficacy of a short-term, manualized, combined group EBP model for PTSD in women OEF/OIF Veterans and a unique structure for providing repeated in-session imaginal exposures for all participants in a group setting.

2. Castillo, D. T., Chee, C. L., Nason, E., & Keller, J. (2013, August). Efficacy of Group Delivered Evidence-Based PTSD Therapies in Female OIF/OEF Veterans. Paper presented at the American Psychological Association Conference, Honolulu, HI.

Abstract. Statement of Problem. Exposure and cognitive treatments are evidence-based psychotherapies (EBPs) for PTSD (Cahill, et. al., 2009). These manualized protocols for PTSD have been examined primarily in an individual format, with group studies fewer and containing methodological problems (Shea, et al., 2009). The only Randomized Controlled Trial (RCT) to include exposure therapy in group format (Schnurr, et al., 2003) failed to find the superiority of combined EBP treatments over Present-Centered Group Therapy. While cognitive therapy can be transferred to a group setting, exposure therapy faces logistic challenges of assuring

repeated imaginal exposure for every member in every group session, as in the individual Prolonged Exposure (PE) model. Castillo's clinical group program (2004) was condensed to a 16-session RCT to examine the overall efficacy of group EBP treatment. The manualized group protocol included exposure, cognitive, and skills blocks, with 3 members in each group. **Subjects.** Subjects were 86 female OIF/OEF Veterans with PTSD. **Measures.** Descriptive: Demographics, Structured Clinical Interview for DSM-IV Axis I and II, Life Events Checklist (LEC), Military Stress Exposure Questionnaire (MSEQ), Health Care Utilization, and medication usage. Primary Outcome: Clinician Administered PTSD Scale (CAPS). Others: Health Related Quality of Life (SF-36), Quality of Life Inventory (QOLI), PTSD Symptom Checklist (PCL), and Health Care Utilization across treatment. **Procedure.** Subjects were assessed and randomized by groups of three into a 16-week treatment group or a 16-week minimal attention/wait-list (WL) arm. Treatment consisted of exposure (5 weeks), cognitive (5 weeks), and skills (assertiveness and relaxation; 4weeks) blocks. The first and last sessions were inactive treatment and block order was controlled. Bi-monthly individual supportive therapy was provided in the WL arm. The PCL was administered between treatment blocks and every four weeks in the WL arm. Follow up assessments were conducted post treatment/WL, and at 3 and 6 months after treatment. **Results.** Demographics reflected a young (*M*=36), educated (*M*=15 yrs), ethnically diverse sample (40% Hispanic, 17% Native American, 31% White). Subjects had high rates of trauma (69%>8 trauma types, 66%>25 trauma incidents, LEC), with combat experience (30-79%), verbal (89%) and physical (63%) sexual harassment (minimum one incident), and sexual assault (46% minimum one incident) in the military (MSEQ). Co-morbidity (77% Axis I, 56% Axis II) and PTSD levels (CAPS *M*=153, *SD*=34) were high. Outcome analysis with the CAPS showed a significant pre/post by treatment interaction ($p<.01$), with a significant 23-point reduction of PTSD symptoms after treatment ($p<.001$). An intent to treat RM-ANOVA showed significant PTSD decreases were sustained at 3- and 6-months ($p<.01$). Secondary outcome analyses will be presented. **Conclusion.** This RCT demonstrates the efficacy of a manualized group EBP model for PTSD, the results of which are maintained 6 months later, in a young, educated, highly traumatized sample of OIF/OEF female Veterans. This study adds scientific rigor to the group literature on the treatment of PTSD using EBPs, with implications for a unique model to deliver exposure therapy in small, 3-member groups similar to the individual PE model.

3. Nason, E., Keller, J., Chee, C. L., & **Castillo, D. T.** (2013, August). Ethnic Differences in Female OIF/OEF Veterans with PTSD. Paper presented at the American Psychological Association Conference, Honolulu, HI.

Abstract. **Statement of Problem.** Research has consistently found the highest PTSD rates among ethnic minorities (Brewin et al. 2000), with a paucity of research on female Veterans (Wolfe, 1993). Females comprise 14% of Operation Iraqi Freedom (OIF) and Operation Enduring Freedom Veterans (OEF; DOD, 2008) and have the highest rates of PTSD (Kessler et al., 1995). Therefore, it is important to examine the extent to which ethnic differences are present among female Veterans. This study compares the clinical presentation among Non-Hispanic White (NHW), Hispanic, and Native American (NA) OIF/OEF female Veterans with PTSD. **Subjects.** Participants were 76 female OIF/OEF Veterans with PTSD and the ethnic makeup was 47% Hispanic, 34% NHW, and 19% NA. **Procedure.** The current study uses data from the baseline assessment from a larger randomized control trial. Participants completed demographics, Life Events Checklist (LEC), and Military Stress Exposure Questionnaire (MSEQ) measures. Psychopathology was assessed with the Structured Clinical Interview for DSM-IV, Axis I and II (SCID-I and II), and Clinician Administered PTSD Scale (CAPS). **Results.** Analyses on demographics revealed no differences among the ethnic groups on age, income, current employment, and marital status. The only significant difference was in years of education, with NHWs (*M*=15.81) higher than Hispanics (*M*=13.70; $p = .002$). The LEC reflected no differences among the three ethnic groups in number of trauma types or total number of trauma incidents. However, on the MSEQ, significant differences were found on two types of

combat trauma. Hispanics ($p < .001$) and NAs ($p = .004$) prepared or evacuated dead bodies more often than NHWs; and NHWs ($p = .005$) and Hispanics ($p = .001$) reported more experiences of dangerous combat duty than NAs. Significant differences in psychopathology were found among the ethnic groups. On the CAPS, Hispanics had higher rates of PTSD than NHWs ($M = 76.78$ versus $M = 63.41$, $p = .026$), which was driven by higher avoidance/numbing symptoms (Hispanics $M = 31.24$; NHWs $M = 24.37$, $p = .019$). NAs also scored higher on avoidance/numbing symptoms than NHWs ($M = 32.13$ versus $M = 24.37$, $p = .043$). On SCID-I, Hispanics had significantly higher rates of obsessive compulsive disorder (OCD) than NHWs ($p = .003$) and NAs ($p = .022$). On SCID-II, Hispanics ($p < .001$) and NAs ($p < .001$) had significantly higher rates of depressive personality disorder than NHWs. **Conclusion.** The present study provides important data on ethnic differences in female OIF/OEF Veterans. Despite the few demographic and trauma characteristic differences, one finding emerged throughout. Hispanics showed higher levels of specific combat experiences, with important diagnostic implications for greater PTSD severity and higher OCD rates. These findings are consistent with results from the National Vietnam Veterans Readjustment study (1988), where Hispanic male Veterans showed highest rates of PTSD among ethnic groups. Finally, the higher rates of Axis II depressive personality disorder in NAs and Hispanics may reflect alternative symptom expression from trauma exposure, rather than PTSD.

4. Castillo, D. T. (2013 August). A Randomized Controlled Trial for Efficacy of Group Delivered Evidence-Based Treatments for PTSD in OIF/OEF Women Veterans. VISN 18 Research Forum, Albuquerque, NM.

Abstract. Statement of Problem. Exposure and cognitive treatments are evidence-based psychotherapies (EBPs) for PTSD (Cahill, et. al., 2009). These manualized protocols for PTSD have been examined primarily in an individual format, with group studies fewer and containing methodological problems (Shea, et al., 2009). The only Randomized Controlled Trial (RCT) to include exposure therapy in group format (Schnurr, et al., 2003) failed to find the superiority of combined EBP treatments over Present-Centered Group Therapy. While cognitive therapy can be transferred to a group setting, exposure therapy faces logistic challenges of assuring repeated imaginal exposure for every member in every group session, as in the individual Prolonged Exposure (PE) model. Castillo's clinical group program (2004) was condensed to a 16-session RCT to examine the overall efficacy of group EBP treatment. The manualized group protocol included exposure, cognitive, and skills blocks, with 3 members in each group. **Subjects.** Subjects were 86 female OIF/OEF Veterans with PTSD. **Measures.** Descriptive: Demographics, Structured Clinical Interview for DSM-IV Axis I and II, Life Events Checklist (LEC), Military Stress Exposure Questionnaire (MSEQ), Health Care Utilization, and medication usage. Primary Outcome: Clinician Administered PTSD Scale (CAPS). Others: Health Related Quality of Life (SF-36), Quality of Life Inventory (QOLI), PTSD Symptom Checklist (PCL), and Health Care Utilization across treatment. **Procedure.** Subjects were assessed and randomized by groups of three into a 16-week treatment group or a 16-week minimal attention/wait-list (WL) arm. Treatment consisted of exposure (5 weeks), cognitive (5 weeks), and skills (assertiveness and relaxation; 4weeks) blocks. The first and last sessions were inactive treatment and block order was controlled. Bi-monthly individual supportive therapy was provided in the WL arm. The PCL was administered between treatment blocks and every four weeks in the WL arm. Follow up assessments were conducted post treatment/WL, and at 3 and 6 months after treatment. **Results.** Demographics reflected a young (M=36), educated (M=15 yrs), ethnically diverse sample (40% Hispanic, 17% Native American, 31% White). Subjects had high rates of trauma (69%>8 trauma types, 66%>25 trauma incidents, LEC), with combat experience (30-79%), verbal (89%) and physical (63%) sexual harassment (minimum one incident), and sexual assault (46% minimum one incident) in the military (MSEQ). Co-morbidity (77% Axis I, 56% Axis II) and PTSD levels (CAPS M=153, SD=34) were high. Outcome analysis with the CAPS showed a significant pre/post by treatment interaction (p<.01), with a significant 23-point

reduction of PTSD symptoms after treatment ($p<.001$). An intent to treat RM-ANOVA showed significant PTSD decreases were sustained at 3- and 6-months ($p<.01$). Secondary outcome analyses will be presented. **Conclusion.** This RCT demonstrates the efficacy of a manualized group EBP model for PTSD, the results of which are maintained 6 months later, in a young, educated, highly traumatized sample of OIF/OEF female Veterans. This study adds scientific rigor to the group literature on the treatment of PTSD using EBPs, with implications for a unique model to deliver exposure therapy in small, 3-member groups similar to the individual PE model.

APPENDIX D—MANUSCRIPTS

1. Main Outcome Manuscript

A Randomized Controlled Trial of Group Delivered Cognitive and Exposure Therapy for PTSD in Women Veterans

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Abstract

Objective: Our purpose was to examine the efficacy of a structured group treatment protocol with blocks of Evidence-Based Psychotherapies (EBP)—cognitive, exposure, skills—for Post-traumatic Stress Disorder (PTSD); and secondarily, to examine the contributions of each treatment on PTSD improvement. **Method:** Eighty-six women Veterans of Afghanistan and Iraq wars were randomized to a 16-week group treatment or minimal attention waitlist condition. Groups contained three members, with waitlist participants offered treatment after waitlist completion. Participants were assessed prior to randomization and after treatment or waitlist; treatment participants were assessed three and six months after treatment with primary (Clinician Administered PTSD Scale, CAPS; Blake, Weathers, Nagy, Kaloupek, Klauminzer, Charney et al., 1990) and secondary outcome measures. The PTSD Symptom Checklist (PCL; Weathers, Litz, Herman, Huska, & Keane, 1993) was administered before and after each of the three treatment blocks within the 16-week protocol. **Results:** Analyses (intention-to-treat, completer, and group as unit of analysis) demonstrated PTSD improvement ($p < .05$) with large effect sizes (Cohen's $d = 0.90$-1.47) for treatment and waitlist-to-treatment crossover participants, with treatment effects maintained 6 months later. Clinical significance showed 10-point CAPS decreases (72-76% participants) and 43-50% with loss of PTSD diagnosis, comparable to individual Prolonged Exposure findings. Finally, PTSD significantly improved with each treatment, exposure significantly more than cognitive and skills. **Conclusions:** This study establishes the efficacy of a unique group protocol for PTSD with blocks of EBP treatments, suggests the greater efficacy of exposure over cognitive and skills conditions, and provides a structure for group exposure therapy.

Key words: PTSD, group treatment, women, cognitive, exposure therapy

A Randomized Controlled Trial of Group Delivered Cognitive and Exposure Therapy for PTSD in Women Veterans

The standard of care for the treatment of Post Traumatic Stress Disorder (PTSD) has been established in exposure and cognitive therapies with Prolonged Exposure (PE) and Cognitive Processing Therapy (CPT) protocols, when delivered in an individual format (Cahill, Rothbaum, Resick, & Follette, 2009; Institute of Medicine [IOM], 2007). While group format for PTSD treatment has been popular in Veterans Affairs (VA; Rosen et al., 2004), support for group delivery lags behind the individual literature (IOM, 2007; U.S. Department of Veterans Affairs & Department of Defense, 2010). A review (Shea, McDevitt-Murphy, Ready, & Schnurr, 2009) and recent meta-analysis (Sloan, Feinstein, Gallagher, Beck, & Keane, 2013) support efficacy, but not effectiveness of group delivered PTSD treatments. The meta-analysis (Sloan et al., 2013) included 16 randomized controlled trials (RCT) of group-delivered cognitive behavioral therapies, which targeted PTSD and/or included a PTSD outcome measure. The findings showed all group treatment interventions significantly improved PTSD, with medium-to-high within treatment effect sizes (Cohen's d = 0.7, range = 0.09-2.16), smaller than in the individual literature (range = 0.40-4.18, Cahill et al., 2009). No differences were found when treatments were compared to active controls, suggesting none of the targeted interventions improved upon the non-specific effects found in a group setting. The authors identified a number of methodological problems in the group literature, as noted in other reports (IOM, 2007; Shea et al., 2009), and include the lack of scientific rigor and standardization in delivery of Evidence-Based Psychotherapies (EBPs), inadequate handing of missing data, and not accounting for clustering effects within groups. Recommendations include conducting RCTs, statistical imputation for missing data (rather than last observation carried forward), and addressing

clustering within groups by calculating Intra-Class Correlation (ICC) and/or analyzing the data with group as the unit of analysis to account for inflation of type I error (Baldwin, Murray, & Shadish, 2005).

Another striking difference between controlled trials in the group and individual literature is the content and length of treatments. Content of PTSD groups typically combine a variety of interventions (e.g., cognitive with assertiveness; Cahill et al., 2009), making it difficult to ascertain the contribution of intervention type to PTSD improvement; and group therapy protocols are not directly comparable to the individual PE or CPT standard of care. One group study implemented the CPT protocol (Chard, 2005), but alternated individual and group sessions, not allowing for the assessment of the group contributions to outcome. One study (Schnurr et al., 2007) provided 2 in-session imaginal exposures to an index trauma per member, far fewer than the 8 exposures in the 10-session PE protocol. While the elements of cognitive restructuring can be implemented in group (e.g., education on cognitive restructuring, modification of distorted cognitions), exposure to an index trauma in a group setting poses unique logistical challenges, specifically, providing repeated in-session imaginal exposures with every member in every session. In a typical 8-member, 90-minute group, only 10 minutes of in-session imaginal exposure could be devoted to each group member, compared to the 30-60 minute imaginal exposures in PE. While the minimum length of in-session imaginal exposure time required to produce habituation has not been established, van Minnen & Foa (2006) reported 30-minute in-session imaginal exposures produced comparable PTSD reductions to 60-minute exposures in an individual therapy trial. Finally, the duration and length of group treatment protocols typically exceed PE (10, 90-minute sessions) and CPT (12, 60-minute sessions). Only 4 of 16 studies reviewed by Sloan et al. (2013) had 12 or fewer sessions, with one as many as 30; and only 7 of

16 group study sessions were 90 minutes or less in length, with some as long as 2.5 hours. With the wide variation in delivery of interventions, methodological problems, and statistical concerns in the group literature, few conclusions can be made about comparability to the individual literature and standard of care for PTSD.

Aside from the issues facing the delivery of specific PTSD treatment interventions in a group setting, the benefits of group therapy have been identified as curative factors that occur in group (e.g., instillation of hope, universality, imparting information, altruism, corrective emotional experience, and catharsis; Yalom, 1995). A group setting for PTSD offers validation of traumatic experiences, normalization of trauma responses, and reduction of isolation (Shea et al., 2009). While group treatments may produce smaller effect sizes, patients report high satisfaction with group treatment (Sloan et al., 2013). Finally, group treatment delivery can address practical issues like increasing efficiency and maximizing limited resources.

This study was developed from a clinical protocol where cognitive, exposure, and skills (behavioral) EBPs were provided in separate groups (Castillo, 2004). The clinical protocol was condensed to a 16-week group with three unique aspects: a) separation of treatment interventions into blocks, b) weekly repeated in-session imaginal exposure for every group member, and c) group membership size of three participants. The small group membership size allowed, for the first time, the application and examination of repeated in-session imaginal exposure therapy in a group setting. The primary aim of this RCT was to examine the overall efficacy of the 16-week protocol on PTSD severity compared to a minimal attention waitlist control in a sample of Afghanistan (Operation Enduring Freedom [OEF]) and Iraq (Operation Iraqi Freedom [OIF]) era women Veterans. The secondary aim of the study was to examine the contribution of each treatment on PTSD improvement. Our hypotheses were: a) the structured EBP group treatment

would improve PTSD symptoms and functioning over a 16-week minimal attention wait-list arm, b) PTSD improvements would be maintained at 3- and 6-month follow-up, and c) the cognitive and exposure treatment blocks would produce greater PTSD changes than the skills block when controlling for order effects.

Method

Participants

Participants were 97 women veterans who served on active duty after September 11, 2001, classified as OEF/OIF service members, and recruited from outpatient mental and medical health clinics at the New Mexico VA Health Care System (NMVAHCS). Study inclusion criterion were: presence of a current PTSD diagnosis, based on the Diagnostic and Statistical Manual for Mental Disorders, 4th edition (DSM-IV; American Psychiatric Association, 1994), stability on psychiatric medications for a minimum of one month, no active drug or alcohol abuse, one clear trauma memory, and agreement not to participate in other PTSD treatments during the study. Inclusion/exclusion criteria were determined at screening and initial assessment. Participants were excluded for less than a three month alcohol/drug dependence remission, presence of psychotic or bipolar/manic symptoms within the past month, cognitive impairment, suicidal/homicidal ideation, involvement in a violent relationship, or engagement in self-mutilation. Of the 97 screened, 11 were excluded (see Figure 1 for participant flow) and of the remaining 86, 44 were randomized to treatment (Tx), and 42 to the minimal attention waitlist (WL) control arm. After completion of the 16-week WL, participants were offered the 16-week treatment protocol (Waitlist-to-Treatment [WLT]) and 25 elected to attend. The average age of the total sample was 35.9 (*SD* = 11.0); 39.5% (*n* = 34) were Hispanic, 31.4% (*n* = 27) non-Hispanic White, and 17.4% (*n* =15) Native American (see Table 1 for full demographic and

baseline characteristics). Participants were reimbursed $75 for initial and $65 for follow-up assessments. The study was approved by the Department of Defense (DoD) and the New Mexico VA Healthcare System at the University of New Mexico Institutional Review Boards.

Measures

Clinician Administered PTSD Scale (CAPS; Blake, Weathers, Nagy, Kaloupek, Klauminzer, Charney et al., 1990). The CAPS, considered the gold standard for the assessment of PTSD, was administered to determine inclusion eligibility and as the primary outcome measure. Based on the DSM-IV (American Psychiatric Association, 1994), the CAPS consists of 17 PTSD symptoms in 3 categories—re-experiencing, avoidance/numbing, and hyperarousal—plus guilt, dissociation, derealization, and depersonalization symptoms. Internal consistency alpha coefficients for the CAPS in the three categories range from 0.73 to 0.85. Convergent validity of CAPS with other measures is moderate to strong, with correlations between the CAPS and the Mississippi Scale (0.70) and Keane's PTSD scale (PK; 0.84) of the MMPI-2 (Weathers, Keane, & Davidson, 2001). Current PTSD symptoms (past month) and lifetime were assessed.

Structured Clinical Interview for DSM-IV-I (SCID-I; Spitzer, Williams, Gibbon, & First, 1995) and **Structured Clinical Interview for DSM-IV-II-Personality Questionnaire (SCID-II-PQ;** Jacobsberg, Perry, & Frances, 1995). Psychiatric co-morbid exclusionary diagnoses (Axis I and Axis II) were assessed with the SCID-I and II, considered the gold standard in the assessment of psychiatric diagnoses. SCID-I is a structured interview with high levels of reliability (Kappas $\geq$ .75) for symptoms, 90% accuracy in diagnosis (Lobbestael, Leurgans, & Arntz, 2011), and superior validity when compared to information from family informants, review of medical records, and observations of clinical staff over other diagnostic interviews (Basco, Bostic, Davies, Rush, Witte, et al. 2000). The SCID-II-PQ is a 20-minute

self-report questionnaire with interviewer follow-up on endorsed items with sensitivity and specificity, a low rate of false negatives compared to the full interview, and an overall kappa of 0.78 (Ball, Rounsaville, Tennen, & Kranzler, 2001).

Life Events Checklist (LEC; Gray, Litz, Hsu, & Lombardo, 2004); **Military Stress Exposure Scale** (MSEQ; Fontana & Rosenheck, 1997). Trauma events were assessed with the LEC and MSEQ. The LEC is a 17-item self-report questionnaire developed with the CAPS (Blake et al., 1990), empirically validated, and found to have high temporal stability for both total and individual items (Gray et al., 2004). Two summary scores for the number of trauma types and number of trauma incidents were summarized from the 17 items. The MSEQ, which captures 14 incidents of combat and sexual traumas experienced by women veterans during military service, was included to supplement the LEC. Eleven items cover combat experiences and three items assess sexual harassment/assault.

Medical Outcomes Study Short Form-36 (SF-36; Ware & Sherbourne, 1992); **Quality of Life Inventory** (QOLI; Frisch, Cornell, Villanueva, & Retzlaff, 1992); **PTSD Symptom Checklist** (PCL; Weathers, Litz, Herman, Huska, & Keane, 1993). The SF-36, QOLI, and PCL were secondary outcome measures. The SF-36 measures social functioning and life quality with the Mental and Physical Component Summary scales. Sensitivity and concurrence has been demonstrated in measuring PTSD change with the SF-36 (Shiner, Watts, Pomerantz, Young-Xu, & Schnurr, 2011). The QOLI measures importance of and satisfaction in 16 life domains for a total life quality score ranging from Very Low to High. Sensitivity to changes in clinical settings has been found with the QOLI and it has been used as an outcome measure in psychiatric populations (Frisch, Clark, Rouse, Rudd, Paweleck, Greenstone et al. 2005). The PCL is a self-report questionnaire, based on the 17 PTSD symptoms and has a high correlation (0.93) with the

CAPS, high internal consistency (Chronbach's alpha = 0.94), a sensitivity of 0.78, specificity of 0.86, and diagnostic efficiency of 0.83 (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996). Finally, health care utilization and medication use, along with demographics were assessed using self-report questionnaires.

Assessment Fidelity

The CAPS and SCID-I structured interviews were video recorded to evaluate fidelity of PTSD and other psychiatric diagnoses, with 15% randomly selected and rated by a trained, independent rater. Current and lifetime CAPS interviews for the initial assessment, and current CAPS for post-treatment, 3-, and 6-month follow-up interviews were reviewed. The intraclass correlation for CAPS severity was 0.98. The κ statistic for SCID-I diagnoses was 0.82, 95% CI [0.75, 0.89].

Procedure

The study was conducted from 2008 to 2013. Volunteers were first screened for eligibility, described the procedures, consented for participation, and administered the assessment interviews and self-report measures. Eligible participants were then randomized by three to either a 16-week Tx or a 16-week WL arm. Outcome assessment was conducted post-treatment and post-waitlist, and at 3- and 6-months for the treatment arm. Subjects in the WL arm were provided bi-monthly supportive counseling sessions, which followed a Present-Centered Therapy model (Schnurr et al., 2007) and excluded active treatment interventions, such as exposure, cognitive, or behavioral interventions. The bi-monthly sessions alternated office and telephone contacts with a study psychologist. At the completion of WL, a subset of participants (n = 25) elected to receive the 16-week treatment, labeled WLT crossovers, and were assessed as in the Tx arm. A total of 14 groups were conducted in the Tx arm and 7 in the WLT crossover

subset; one group in each of the Tx and WLT arms dissolved, the former by the study staff due to one drop out and one disruptive patient and the latter due to drop outs.

Assessments were conducted by masters and bachelor's level trained assessment technicians (AT), blind to randomization. All treatment groups were conducted by a doctoral level psychologist and the exposure block was co-facilitated by an AT; blinding was maintained by excluding the AT from future assessments for participants in their group.

Treatment Protocol

The treatment arm was a 16-week, three-block treatment protocol, with 5 sessions of exposure therapy, 5 of cognitive restructuring therapy, and 4 of behavioral skills training. Session 1 and 16 were not considered active treatment sessions. Session one included an orientation with education on EBPs for PTSD and session 16 was for wrap-up and discussion of future directions. The three treatment blocks were randomized into 6 possible orders. Session 1 of the exposure block included education on the theory of exposure therapy, identification of coping strategies, selection of the index trauma, and instructions for writing a trauma narrative for subsequent sessions. Sessions 2-5 consisted of in-session imaginal exposure to the index trauma for approximately 30 minutes with each group member (Castillo, C'de Baca, Qualls, & Bornovalova, 2012). The exposure protocol was a modification of two protocols (Foa, Hembree, & Rothbaum, 2007; Keane, Fairbank, Caddell, & Zimering, 1989). In-session imaginal exposure consisted of the participant reading aloud the written trauma narrative followed by guided exposure through the index trauma once, with the therapist eliciting sensory experiences, slowing the pace at the most difficult points, and soliciting anxiety ratings. Hot spots (repeated review of worst parts of the trauma) and in-vivo exposure (practicing avoided situations between sessions)

from the PE protocol were not included. Homework consisted of weekly re-writing of the trauma narrative and, in weeks 4-5, group members were to read the written trauma narrative daily.

The 5-session cognitive block implemented cognitive restructuring based on the CPT model (Resick & Schnicke, 1993). Session 1 included education on the impact of negative, distorted cognitions on emotions, particularly in PTSD. In sessions 2-5, the five themes of safety, trust, power/control, esteem, and intimacy from CPT were reviewed, one per week, with esteem and intimacy combined in the final session. Weekly homework consisted of participants writing on the impact of the trauma on their beliefs, one theme per week. In session, each member read aloud the writings, with distorted beliefs challenged by the therapist and members and modified to realistic/neutral beliefs. Excluded was trauma writing/review, as in CPT.

The 4-session skills block consisted of assertiveness (Lange & Jakubowski, 1976) and relaxation training. Assertiveness training in session 1 and 2 involved didactics, defining and differentiating assertive from aggressive and passive behaviors and tactics for behavioral change. Sessions 3 and 4 involved videotaped assertiveness role-play, with viewing and feedback provided to participants in the same session to shape assertive behaviors. One of 4 relaxation techniques (breathing retraining, sensory focusing, progressive deep muscle relaxation, and thought stopping) was reviewed and practiced in the last half hour of each session. Daily homework consisted of relaxation practice, with pre/post anxiety ratings.

The study psychologists were trained and supervised with training tapes developed by the first author based on the structured clinical protocol (Castillo, 2004). All groups were scheduled to meet weekly for 90 minutes and the range of time for group completion was 16-20 weeks.

Treatment Fidelity

Group sessions were video recorded and essential elements for each treatment block were identified by the first author and two study psychologists to capture therapist adherence. Fifteen percent of treatment blocks, independent of the group in which it was provided, were selected for review. Three cognitive and skills groups and 4 exposure groups were selected for review. Therapists adhered to 99% of the essential elements in the exposure, 94% in the cognitive, and 91% in the skills treatments.

Treatment Dose and Individual Make-up Sessions

Treatment dose in completer participants (Tx + WLT = 48) ranged from 86-100% with 86% treatment dose in 5 (11%) participants (missed 2 sessions), 93% treatment dose in 16 (33%) participants (missed one session), and 100% (14 active therapy sessions) treatment dose in 27 participants (56%). Overall attendance was high, with only 4% of sessions missed. Individual make-up sessions were provided in 2% (11 individual make-up sessions) of the 672 total sessions (14 active treatment sessions x 48 total participants) for 8 subjects to assure continuity of content in the group sessions. The 11 make-up sessions were provided most often in the cognitive and skills treatments (5 sessions each) and the least in exposure treatment (1 session).

Data Analysis

The baseline and demographic data were analyzed comparing the Tx arm participants to the WL arm and to the WLT subset using Fisher's exact test for categorical variables and Satterwaite's corrected *t* test for continuous variables. As dropouts exceeded 10% (Tx = 27%, WL = 17%, WLT = 36%), an Intention-to-Treat (ITT) analysis (IOM, 2007) was conducted on current CAPS, the primary outcome measure for PTSD, using SAS Proc Multiple Imputation (MI) programming to impute missing values for post (Tx = 12, WL = 8, WLT = 9) and follow-up (3-month: Tx = 13, WLT = 10; 6-month: Tx = 13, WLT = 11) for the full data set (Tx = 44, WL

= 42, WLT = 25). Next, Proc MIANALYZE was used to combine 50 imputations and was utilized throughout the ITT analyses, as 200 imputations produced similar results. Given the ITT analyses resulted in significant improvement in PTSD in the Tx arm and WLT subset, subsequent analyses for primary (CAPS) and secondary (QOLI, SF-36) outcomes were conducted in completer samples. Repeated Measures Analysis of Variance (RM-ANOVA) using SAS Proc Mixed programming was conducted to examine interaction, pre/post differences in Tx, WL, and WLT samples and longitudinal differences between and within Tx and WLT arms. Post hoc analyses were computed using paired *t* tests. RM-ANOVA was computed for group as the unit of analysis with similar post hoc testing. SAS 9.3 was used for all analyses.

Results

The demographic and baseline characteristics for the Tx and WL arms, and WLT subset are presented in Table 1. No significant differences were found between the Tx and WL arms and the Tx and WLT conditions except on total number of Axis I diagnoses ($p = .02$). Tx arm participants had significantly more diagnoses than the WL participants.

Intention-to-Treat Outcome Analysis

The ITT analyses included all study participants (Tx = 44, WL = 42, WLT = 25 subset) with the Tx arm compared to the WL and WLT in separate RM-ANOVA analyses and with imputation of missing values in two 2 x 2 (Tx/WL x pre/post; and Tx/WLT x pre/post) analyses on current CAPS as the dependent variable. A significant interaction was found in the Tx/WL x pre/post comparison ($F(1,84) = 3.70$, $p < .001$) with post hoc *t* tests showing a significant decrease in CAPS for Tx ($p < .001$) and no change in the WL arm ($p = .34$; see Figure 2a). A significant interaction was not found in the Tx/WLT x pre/post comparison ($F(1,67) = 0.69$, $p = .62$), with significant post hoc *t* test decreases in both Tx (see above) and WLT ($p = .005$) scores.

A RM-ANOVA was computed on longitudinal data for post, 3-, and 6-month follow-up assessments for the Tx and WLT arms, which were not significantly different ($p = 0.44$). Post hoc analyses within each arm showed no significant differences in CAPS scores among follow-up assessments for Tx arm (post and 3-month: $p = .92$; post and 6-month: $p = .82$). The WLT arm also showed no significant difference between post and 3-month assessment ($p = .36$), but a significant decrease was found between the post and 6-month ($p = .05$) assessment (see Figure 2a). The ITT findings suggest improvement with the 16-week treatment for both Tx and WLT conditions with effects maintained at 3- and 6-month follow-up for the Tx arm and further decreases from post to 6-month assessment for the WLT subset.

Completer Outcome Analysis

Two 2 x 2 (Tx/WL x pre/post; and Tx/WLT x pre/post) RM-ANOVA analyses were computed on current CAPS as the dependent variable in the completer sample (Tx = 32, WL = 35, WLT = 16) and, as in the ITT, a significant interaction was found in the Tx/WL x pre/post comparison ($F(1,65) = 3.92$, $p < .001$), with post hoc t tests significant for decreases in the Tx arm ($p < .001$), but not the WL arm ($p = .49$). Longitudinal changes were examined using a RM-ANOVA within the Tx arm across post, 3- and 6-month follow-up assessments, with no significant differences found ($p = .99$), suggesting improvement after the 16-week group was maintained 3 and 6 months after treatment. The 2 x 2 Tx/WLT x pre/post RM-ANOVA comparison on current CAPS as the dependent variable was computed and no significant interaction ($F(1,46) = 0.12$, $p = .73$) was found, with significant post hoc t test decreases found in both conditions (Tx: $p < .001$; WLT: $p = .01$) at post assessment. There were no significant differences among post, 3- and 6-month assessments within each arm (Tx: $p = .98$; WLT: $p = .79$; see Figure 2b and Table 2). Findings suggest completer participants in both Tx and WLT

crossovers improved with the 16-week treatment to a similar extent and showed comparable maintenance of treatment efficacy.

The secondary outcome measures—QOLI and SF-36—were analyzed each with two 2 x 2 (Tx/WL x pre/post; and Tx/WLT x pre/post) RM-ANOVA analyses. For the total QOLI score, a significant interaction was not found ($F(1,63) = 1.08$, $p = .28$) in the Tx/WL x pre/post comparison, with significant pre/post differences found for both the Tx ($p = .005$) and WL ($p = .03$) arms, indicating improvement in quality of life after the 16 weeks of treatment and waitlist conditions. In the longitudinal RM-ANOVA analyses within the Tx arm, significant differences were not found across post, 3-, and 6-month assessments ($p = .30$), suggesting the changes found at post assessment were maintained after treatment. A 2 x 2 (Tx/WLT x pre/post) RM-ANOVA was computed and a significant interaction was not found ($F(1,46) = 0.13$, $p = .72$) nor were significant improvements found for pre/post within the WLT arm ($p = .07$), or in longitudinal RM-ANOVA analyses within the WLT arm ($p = .35$; see Table 2). The findings suggest that while the Tx and WL improved quality of life on the QOLI, the WLT did not.

On the SF-36, two 2 x 2 (Tx/WL x pre/post; and Tx/WLT x pre/post) RM-ANOVA were computed separately for the Mental and Physical Component Summary scales. In the Tx/WL x pre/post analysis, a significant interaction was found for both Mental ($F(1,64) = 8.38$, $p = .005$) and Physical Components ($F(1,64) = 5.64$, $p = .02$), with post hoc t - tests showing significant improvement in the Tx arm (Physical: $p = .001$; Mental: $p < .001$), but not the WL arm (Physical: $p = .62$; Mental: $p = .21$). The longitudinal RM-ANOVA across post, 3-, and 6-month assessments within the Tx arm was not significant for Physical ($p = .87$) or Mental ($p = .44$) Components (see Table 2), suggesting maintenance of treatment effects. Next, the 2 x 2 (Tx/WLT x pre/post) RM-ANOVA was computed, with no significant interactions for either the

Physical ($F(1,46) = .001$, $p = .95$) or Mental ($F(1,46) = .02$, $p = .90$) Components, nor was a significant difference found between the two arms (Physical: $p = .61$; Mental: $p = .59$). Post hoc t tests showed significant improvements in both treatments (Tx, see above; WLT: Physical $p = .02$, Mental $p = .006$). The longitudinal analyses across post and follow-up assessments within the WLT arm was not significant for Physical ($p = .58$) or Mental ($p = .14$) Components. The results suggest both Mental and Physical Components of the SF-36 improve with group treatment for both Tx and WLT, and effects are maintained 3 and 6 months after treatment (see Table 2).

Clinical Improvement

Clinical PTSD improvement was measured by several indicators (Schnurr, Friedman, Engle, Foa, Shea, Chow et al. 2007) including: a) response to treatment, defined as a 10-point decrease in current CAPS, b) a 20-point decrease in current CAPS, c) loss of diagnosis, defined as current CAPS less than 45 and below DSM-IV diagnostic symptom criteria, and d) complete remission, defined as current CAPS less than 20. In the Tx arm, 75% showed a response to treatment, 59% a 20-point drop in CAPS, 50% a loss of PTSD diagnosis, and 25% in total remission. The results in the WLT subset were consistent with the Tx arm, but slightly more variable (see Table 3). Clinical improvement was similar to individually delivered PE in a 10-session protocol (Schnurr et al., 2007), where 75% experienced a response to treatment; 47% a loss of diagnosis; and 22% in total remission in the completer sample.

Group as Unit of Analysis

Baldwin et al. (2005) identified the violation of the assumption of independence of observations in statistical analyses and clustering effects within groups as problematic in group outcome trials. Both clustering and lack of independence of observations inflate type I errors,

leading to exaggerated findings. When Baldwin et al. (2005) conservatively reanalyzed Evidence Supported Treatment studies provided in group, 12-68% were no longer statistically significant. The authors recommend Intra-Class Correlation (ICC) calculations for power analyses in estimating sample size and in outcome analyses. As ICC was not included at the study outset, we calculated an estimated ICC and re-analyzed the data using the group as the unit of analysis, rather than the individual, to address lack of independence of observations. As the Tx and WLT arms were not statistically different on the CAPS in the individual analyses, the two were combined for 19 completer groups (Tx = 13, WLT = 6). An ICC computed on the CAPS with a variance component analysis resulted in a 0.27 variance due to group, suggesting small to moderate group effects contributing to PTSD outcome. A RM-ANOVA was computed on CAPS scores with the 19 groups across 2 assessments (pre/post), and was found significant ($F(1,18) = 33.99$, $p < .001$). Cohen's *d* pre/post effect size was 1.42 and follow-up analysis showed no significant difference across post, 3-, and 6-month assessments. The results support the individual analyses, with improvement after treatment, maintained 3 and 6 months later (see Table 4 for details).

Treatment Comparisons

The secondary aim of the study was to examine contributions to PTSD change by each treatment type—exposure (E), cognitive (C), skills (S)—as measured by the PCL between blocks within the 16-week protocol. Treatment type and order effects were examined in a 3 (cognitive, exposure, skills) x 6 (CES, CSE, ECS, ESC, SCE, SEC) RM-ANOVA on pre/post PCL with Tx and WLT arms combined and individual as the unit of analysis ($n = 45$). The 6 possible treatment orders were randomly assigned in the 19 groups and the order distribution was as follows: 5 CES, 3 CSE, 3 ECS, 2 ESC, 4 SCE, and 2 SEC groups. A significant interaction between

treatment and order was not found (p = .65), nor was a main effect found for order (p = .84). However, a significant main effect for treatment was found (p = .04), suggesting that, while overall treatment improved PTSD, the findings were not influenced by order (see Table 5). Post hoc t tests showed each treatment significantly lowered the PCL (cognitive: delta = 4.38 points; p = .006; exposure: delta = 8.59 points; p < .001; and skills: delta = 3.89 points; p = .004). Comparisons between the treatments showed the exposure block decreases were significantly greater than the cognitive (p = .05) and skills (p = .02) treatments, with no differences between the cognitive and skills (p = .64). The exposure treatment also had the largest within treatment effect size (Cohen's d: E = 0.80, C = 0.43, S = 0.46; see Table 5). Finally, although the order in which each of the treatments were provided was not significant, when the position of each treatment (offered 1st, 2nd, or 3rd) was examined, a significant difference was found (p < .01), with all treatments performing poorest when offered second in the treatment sequence, suggesting the optimal position for treatment was first or last (see Table 5).

Discussion

This RCT demonstrated efficacy for a combined structured group protocol for PTSD with blocks of cognitive-, exposure-, and skills-based EBPs provided in a 3-member group format in a sample of OEF/OIF women veterans. Efficacy was demonstrated with intention-to-treat, completer, and group-unit analyses, providing multiple approaches to support the veracity of the results of this unique protocol. Life functioning also improved with treatment. Further, the study design addresses the many methodological and statistical issues that have plagued the group literature. First, treatments were more closely aligned with the individual EBP protocols, albeit shorter, by implementing the basics of CPT in the cognitive block and repeated in-session imaginal exposures of PE in the exposure block. The separation of interventions allowed for and

showed the impact of each treatment on PTSD improvement. A conservative statistical program for imputing missing values was used in the ITT analysis, rather than last observation carried forward, which has been criticized (IOM, 2007). In addition, we addressed clustering within each group by computing variance inflation with ICC (Baldwin, et al., 2005), which resulted in a larger effect size than individual analyses, and by using the group as the unit of analysis.

Clinical significance, using several indicators, was comparable to individual PE (Schnurr et al., 2007), showing the clinical utility of the group protocol. Regarding each treatment block, all improved PTSD with the largest effect size for exposure, and with exposure better than cognitive and skills treatments. While our hypothesis that both exposure and cognitive treatments would be superior to skills was not supported, the differences are promising, in that this is the first demonstration of superiority of one treatment over another in a group setting. However, this finding should be interpreted cautiously due to the lack of independence in the study design (same subjects received all the treatments), and because the treatments were provided contiguously, such that effects from one treatment could have bled into the others. Clearly, an RCT comparing treatments is necessary to conclusively determine treatment superiority in group. Although order did not contribute to the results, the significant finding of all three treatments performing poorest when delivered second in position is in need of explanation.

In addition to the study's contributions to the group literature, this is the first RCT to provide repeated in-session imaginal exposures in a group, expanding the 2 provided in Trauma Focused Group Therapy (TFGT; Schnurr, Friedman, Foy, Shea, Hsieh, Lavori, et al., 2003) to 4. While repeated between-session exposures in TFGT were required as homework, dose of exposure is ultimately controlled by in-session exposures. Our findings highlight the robust effects of exposure therapy, especially as the 4 in-session imaginal exposures produced clinical

results comparable to PE without the elements of in-vivo exposure and review of hot spots. Therefore, our study suggests variations in PE deserve examination, with the caveat that adherence to the basic principles and theoretical underpinnings of exposure therapy is maintained (Foa, & Kozak, 1986). While other benefits of group, such as curative factors and economic savings were not measured in the study, future studies could shed light on these and other variables such as cohesion and stigma, which could identify the relative value of group versus individual therapy for PTSD. Finally, the small 3-member group is likely to be more appealing than larger groups for the sharing of trauma details. An effectiveness study using an active control, such as present-centered therapy would be a next step for future research. Additionally, a direct comparison of a 10-session group exposure model to the individual PE standard of care would provide information on the utility of group, the benefits and costs in both approaches to PTSD treatment, and the type of modality (group/individual) most appropriate for individuals with PTSD.

A potential limitation is the inclusion of individual sessions, which could confound the positive effects of group treatment. A confound was unlikely, given only 2% of the total sessions were provided individually and 10 of the 11 individual sessions were provided in the cognitive and skills blocks, both of which had smaller PCL changes and effect sizes than exposure group.

The study design and efficacy findings have set the stage for future studies for group interventions for PTSD by more closely modeling individual EBP protocols. Future group studies may shed light on the characteristics of PTSD and individuals most likely to benefit from group or individual EBPs and identify the factors that contribute to PTSD change in the EBP protocols.

References

American Psychiatric Association. (1994). *Diagnostic and statistical manual for mental disorders* (4th ed.). Washington, D.C: Author.

Baldwin, S. A., Murray, D. M., & Shadish, W. R. (2005). Empirically supported treatments or type I errors? Problems with the analysis of data from group-administered treatments. *Journal of Consulting and Clinical Psychology*, *73*, 294-935.

Ball, S. A., Rounsaville, B. J., Tennen, H., & Kranzler, H. R. (2001). Reliability of personality disorder symptoms and personality traits in substance-dependent inpatients. *Journal of Abnormal Psychology*, *110*, 341-52.

Basco, M. R., Bostic, J. Q., Davies, D., Rush, A. J., Witte, B., Hendrickse, W., & Barnett, V. (2000). Methods to improve diagnostic accuracy in a community mental health setting. *American Journal of Psychiatry*, *157*, 1599-1605.

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Klauminzer, G., Charney, D. S., & Keane, T. M. (1990). A clinical rating scale for assessing current and lifetime PTSD: The CAPS-1. *Behavior Therapist*, *18*, 187-188.

Blanchard, E. B., Jones-Alexander, J., Buckley, T. C., & Forneris, C. A. (1996). Psychometric properties of the PTSD Checklist (PCL). *Behaviour Research and Therapy*, *34*, 669 - 673.

Cahill, S. P., Rothbaum, B. O., Resick, P., & Follette, V. M. (2009). Cognitive-behavioral therapy for adults. In E. B. Foa, T. M. Keane, M. J. Friedman, & J. A. Cohen (Eds.), *Effective treatments for PTSD: Practice Guidelines from the International Society for Traumatic Stress Studies* (pp. 139-222). New York: The Guildford Press.

Castillo, D. T. (2004). Systematic outpatient treatment of sexual trauma in women: Application of cognitive and behavioral protocols. *Cognitive and Behavioral Practice*, *11*, 352-365.

Castillo, D. T., C'de Baca, J., Qualls, C., Bornovalova, M. A. (2012). Group Exposure Therapy Treatment for Post-traumatic Stress Disorder in Female Veterans. *Military Medicine*, *177(12)*, 1486-1491.

Chard, K. M. (2005). An evaluation of cognitive processing therapy for the treatment of posttraumatic stress disorder related to childhood sexual abuse. Journal of Consulting and Clinical Psychology, 73, 965-971.

Foa, E. B., Hembree, E. A., & Rothbaum, B. O., (2007). *Prolonged exposure therapy for PTSD: Emotional processing of traumatic experiences—Therapist guide*. New York: Oxford University Press.

Foa, E. B., & Kozak, M. J. (1986). Emotional processing of fear: Exposure to corrective information. *Psychological Bulletin*, *99*, 20-35.

Fontana, A. & Rosenheck, R. (1997). *Women under stress: Evaluation of the Women's Stress Disorder Treatment Teams*. West haven, CT: VA Northeast Program Evaluation Center and National Center for PTSD.

Frisch, M. B., Cornell, J., Villanueva, M. & Retzlaff, P. J. (1992). Clinical validation of the Quality of Life Inventory: A measure of life satisfaction for use in treatment planning and outcome assessment. *Psychological Assessment*, *4*, 92-101.

Frisch, M. B., Clark, M. P., Rouse, S. V., Rudd, M. D., Paweleck, J. K., Greenstone, A., & Kopplin, D. A. (2005). Predictive and Treatment Validity of Life Satisfaction and the Quality of Life Inventory. *Assessment, 12*, 66-78.

Gray, M. J., Litz, B. T., Hsu, J. L., & Lombardo, T. W. (2004). Psychometric properties of the life events checklist. *Assessment*, *11*, 330-341.

Jacobsberg L, A., Perry, S., & Frances, A. (1995). Diagnostic agreement between the SCID-II screening questionnaire and the Personality Disorder Examination. *Journal of Personality Assessment*, *65*, 428-433.

Institute of Medicine (IOM). (2007). *Treatment of Posttraumatic Stress Disorder: An Assessment of the Evidence*. Washington, DC: The National Academies Press.

Keane, T. M., Fairbank, J. A., Caddell, J. M., & Zimering, R. T. (1989). Implosive (flooding) therapy reduces symptoms of PTSD in Vietnam combat Veterans. *Behavior Therapy*, *20*, 245-260.

Lange, A. J. & Jakubowski, P. (1976). *Responsible Assertive Behavior: Cognitive/Behavioral Procedures for Trainers.* Illinois: Research Press.

Levitt, J. T. & Cloitre, M. (2005). A Clinician's Guide to STAIR/MPE: Treatment for PTSD Related to Childhood Abuse. *Cognitive and Behavioral Practice*, *12*, 40-52.

Resick, P. A. & Schnicke, M. K. (1993). *Cognitive processing therapy for rape victims: A treatment manual*. Newbury Park, CA: Sage.

Rosen, C. S., Chow, H. C., Finney, J. F., Greenbaum, M. A., Moos, R. H., Sheikh, J. I., & Yesavage, J. A. (2004). VA practice patterns and practice guidelines for treating posttraumatic stress disorder. *Journal of Traumatic Stress*, *17*, 213-222.

Schnurr, P. P., Friedman, M. J., Foy, D. W., Shea, M. T., Hsieh, F. Y., Lavori, P. W., Glynn, S. M., Wattenberg, M, & Bernardy, N. (2003). Randomized trial of trauma-focused group therapy for posttraumatic stress disorder. *Archives of General Psychiatry*, *60*, 481-489.

Schnurr, P. P., Friedman, M. J., Engle, C. C., Foa, E. B., Shea, M. T., Chow, B. K., Resick, P. A., Thurston, V., Orsillo, S. M., Haug, R., Turner, C., & Bernardy, N. (2007). Cognitive behavioral therapy for posttraumatic stress disorder in women: A randomized controlled trial. *Journal of American Medical Association*, *297*, 820-830.

Shea, M. T., McDevitt-Murphy, M., Ready, D. J., & Schnurr, P. P., (2009). Group therapy. In E. B. Foa, T. M. Keane, M. J. Friedman, & J. A. Cohen (Eds.), *Effective treatments for PTSD: Practice Guidelines from the International Society for Traumatic Stress Studies* (pp. 306-326). New York: The Guildford Press.

Shiner B., Watts, B. V., Pomerantz, A., Young-Xu, Y., & Schnurr, P. P. (2011). Sensitivity of the SF-36 to PTSD Symptom Change in Veterans. *Journal of Traumatic Stress*, *24*, 111–115.

Sloan D. M., Feinstein B. A., Gallagher M. W., Beck J. G., & Keane T. M. (2013). Efficacy of group treatment for posttraumatic stress disorder symptoms: A meta-analysis. *Psychological Trauma: Theory, Research, Practice, and Policy*, *5*, 176–183.

Spitzer, R. L., Williams, J. B., Gibbon, M., & First, M. B. (1995). *Structured Clinical Interview for DSM-IV—Patient Version (SCID-P, Version 2.0)*. Washington, DC: American Psychiatric Press.

U.S. Department of Veterans Affairs & Department of Defense. (2010). VA/DoD clinical practice guidelines for management of post-traumatic stress. Retrieved from http://www.healthquality.va.gov/PTSD-FULL-2010c.pdf

van Minnen, A. & Foa, E. B. (2006). The effect of imaginal exposwure length on outcome of treatment for PTSD. *Journal of Traumatic Stress*, *19*, 427-438.

Ware, J. E. & Sherbourne, C. D. (1992). The MOS 36-Item Short-Form Health Survey (SF-36): I. Conceptual framework and item selection. *Medical Care*, *30*, 473-483.

Weathers, F. W., Keane, T. M., & Davidson, J. R. T. (2001). Clinician-Administered PTSD Scale: A review of the first ten years of research. *Depression and Anxiety, 13*, 132-156.

Weathers, F. W., Litz, B. T., Herman, D. S., Huska, J. A., & Keane, T. M. (1993, October). *The PTSD checklist (PCL): Reliability, validity, and diagnostic utility*. Paper presented at the 9th Annual Meeting of the International Society for Traumatic Stress Studies, San Antonio, TX.

Yalom, I. (1995). *The Theory and Practice of Group Psychotherapy* (4th Ed.). New York: Basic Books.

Table 1. Demographic and Baseline Characteristics of Treatment (*n* = 44), Wait List (*n* = 42), and Wait List to Treatment (*n* = 25) Participants

Characteristics	Treatment Arm *n* (%)	Wait List Arm *n* (%)	Wait List to Treatment *n* (%)
Age, mean years (*SD*) [CI]	36.7 (12.6)	35.1 (9.2)	36.8 (9.3)
	[32.9 to 40.5]	[32.3 to 38.0]	[33.0 to 40.6]
Race/Ethnicity			
Non-Hispanic White	12 (28.6)	15 (34.1)	5 (20.0)
Hispanic	18 (42.9)	19 (43.2)	11 (44.0)
Native American	7 (16.7)	8 (18.2)	6 (24.0)
Other	5 (11.9)	2 (4.6)	3 (12.0)
Married/Cohabitating	23 (52.3)	17 (40.5)	10 (40.0)
Education, mean years (*SD*) [CI]	14.5 (2.2)	14.9 (2.6)	15.4 (2.8)
	[13.8 to 15.1]	[14.1 to 15.7]	[14.2 to 16.6]
Unemployed	17 (38.6)	21 (50.0)	12 (48.0)
Life Events Checklist♦			
8-17 trauma types	31 (70.5)	29 (69.1)	16 (64.0)
≥ 25 trauma incidents	28 (63.6)	29 (69.1)	17 (68.0)
Military Stress Exposure Questionnaire			
≥ 1 month combat environment†	34 (77.3)	34 (81.0)	21 (84.0)
≥ 1 military sexual assault	21 (47.7)	19 (45.2)	13 (52.0)
≥ 1 times physical harassment	26 (59.1)	28 (66.7)	7 (72.0)

≥ 1 times verbal harassment	39 (88.6)	38 (90.5)	23 (92.0)
Head Injury	15 (34.1)	16 (40.0)	13 (54.2)
PTSD disability			
Approved	11 (25.0)	4 (9.8)	3 (12.5)
Pending	11 (25.0)	16 (39.0)	9 (37.5)
Denied	4 (9.1)	2 (4.9)	2 (8.3)
Never Applied	18 (40.9)	19 (46.3)	10 (41.7)
History of Psychiatric Treatment			
Inpatient, mean days (*SD*) [CI]	2.8 (10.0)	6.2 (0.5 to 14.7)	6.0 (19.7)
	[-0.3 to 5.8]	[0.5 to 11.8]	[-2.2 to 14.1]
Outpatient, mean visits (*SD*)	19.4 (34.0)	30.3 (57.4)	38.0 (70.6)
[CI]	[8.4 to 30.4]	[11.9 to 48.6]	[8.2 to 67.8]
Current co-morbid Axis I psychiatric disorder*			
Mood disorder	30 (68.2)	23 (54.8)	13 (52.0)
Anxiety disorder	29 (65.9)	23 (54.8)	14 (56.0)
Substance use/abuse	2 (4.6)	1 (2.4)	0
Current co-morbid Axis II psychiatric disorder			
Cluster A	24 (54.6)	18 (42.9)	9 (36.0)
Cluster B	10 (22.7)	7 (16.7)	3 (12.0)
Cluster C	8 (18.2)	8 (19.1)	3 (12.0)
Psychological Measures			
CAPS, current, mean (*SD*) [CI]	70.6 (19.9)	73.7 (20.0)	72.4 (16.4)
	[64.6 to 76.6]	[67.5 to 80.0]	[65.7 to 79.2]

QOLI, mean (*SD*) [CI]	1.8 (1.0)	1.6 (1.0)‡	1.5 (0.8)‡
	[1.5 to 2.2]	[1.3 to 1.9]	[1.2 to 1.9]
SF-36, mean (*SD*) [CI]			
Physical Component	52.4 (24.8)	47.7 (22.1)	47.7 (22.3)
	[44.8 to 59.9]	[40.8 to 54.5]	[38.5 to 56.9]
Mental Component	38.2 (48.2)	31.7 (23.6)	32.8 (23.7)
	[23.6 to 52.9]	[24.4 to 39.1]	[23.1 to 42.6]

Note. Cell values reflect participant numbers and percentages in parentheses unless otherwise indicated. * $p = .02$. ♦Reflect trauma events experienced and witnessed. †Combat environment was highest of all combat items. ‡ $n = 41$ in WL and $n = 24$ in WLT arms. *M* = Mean; *SD* = Standard Deviation; CI = 95% Confidence Interval; CAPS = Clinician Administered PTSD Scale; QOLI = Quality of Life Inventory; SF-36 = Medical Outcomes Study Short Form-36.

Table 2. Primary (CAPS) and Secondary (QOLI, SF-36) Outcomes in Completer Subjects (Tx: *n* = 32, WL = 35, WLT = 16)

Outcome Measure	Pre/Post *ES*	Pre	Post	3-month	6-month
		M (SD) [95% CI]	*M (SD)* [95% CI]	*M (SD)* [95% CI]	*M (SD)* [95% CI]
CAPS					
Tx	1.05	70.59 (18.4) [63.95 to 77.24]	47.69 (24.6)*** [38.83 to 56.55]	47.03 (26.2) [37.43 to 56.63]	47.42 (26.9) [35.57 to 57.27]
WL	*ns*	69.9 (18.2) [63.7 to 76.2]	67.5 (24.8) [59.0 to 76.0]		
WLT	0.90	72.56 (12.2) [66.08 to 79.05]	52.88 (28.4)* [37.7 to 68.01]	46.40 (26.7) [31.63 to 61.17]	48.64 (24.8) [34.34 to 62.95]
QOLI					
Tx	0.50	1.81 (1.1) [1.43 to 2.20]	2.34 (0.9)** [2.02 to 2.67]	1.97 (1.0) [1.62 to 2.32]	2.24 (1.1) [1.83 to 2.66]
WL	0.19	1.67 (1.0) [1.32 to 2.02]	1.97 (1.6)* [1.58 to 2.36]		
WLT	*ns*	1.69 (0.9) [1.22 to 2.15]	2.38 (1.09) [1.80 to 2.96]	2.13 (1.2) [1.48 to 2.79]	2.07 (1.1) [1.41 to 2.73]
SF36					
<u>Physical</u>					
Tx	0.40	50.55 (24.6) [41.68 to 59.41]	60.67 (26.1)*** [51.27 to 70.08]	58.22 (25.0) [49.05 to 67.39]	61.52 (24.5) [52.53 to 70.52]

WL	*ns*	50.6 (21.6)	51.8 (21.5)		
		[43.1 to 58.1]	[44.3 to 59.3]		
WLT	0.69	53.47 (20.0)	64.32 (26.0)*	54.28 (23.3)	56.05 (27.9)
		[42.82 to 64.11]	[50.45 to 78.20]	[41.40 to 67.17]	[39.94 to 72.16]
Mental					
Tx	0.96	33.20 (18.9)	53.31 (22.7)***	47.47 (23.4)	46.33 (23.1)
		[26.40 to 40.00]	[45.12 to 61.51]	[38.91 to 56.04]	[37.85 to 54.82]
WL	*ns*	35.6 (24.5)	40.2 (21.5)		
		[27.0 to 44.1]	[32.7 to 47.7]		
WLT	0.80	36.86 (19.0)	55.85 (22.1)**	52.84 (27.1)	49.28 (27.5)
		[26.74 to 46.99]	[44.07 to 67.62]	[37.81 to 67.87]	[33.40 to 65.15]

Note. $^{*}p < .05$; $^{**}p < .01$; $^{***}p < .001$ for post hoc within arm paired comparisons. *M* = Mean; *SD* = Standard Deviation; CI = 95% Confidence Interval; *ES* = Effect Size (Cohen's *d*); *ns* = non-significant; Tx = Treatment Arm; WL = Wait List Arm; WLT = Wait List to Treatment crossovers. CAPS = Clinician Administered PTSD Scale; QOLI = Quality of Life Inventory; SF-36 = Medical Outcomes Study Short Form-36.

Table 3. Number (and Percent) of Participants with PTSD Clinical Improvement on CAPS in Completer Subjects

	Response to Treatment *n* (%)	> 20-point decrease *n* (%)	Loss of Diagnosis *n* (%)	Total Remission *n* (%)
Tx Arm				
Post (*n* = 32)	24 (75.0)	19 (59.4)	14 (50.0)	5 (15.6)
3 mo. (*n* = 31)	22 (71.0)	17 (54.8)	14 (50.0)	7 (22.6)
6 mo. (*n* = 31)	22 (71.0)	17 (54.8)	12 (44.4)	5 (16.1)
WLT				
Post (*n* = 16)	10 (62.5)	7 (43.8)	6 (37.5)	3 (18.8)
3 mo. (*n* = 15)	12 (80.0)	10 (66.7)	9 (60.0)	1 (6.7)
6 mo. (*n* = 14)	10 (71.4)	8 (57.1)	5 (35.7)	2 (14.3)

Note. Response to Treatment: > 10-point decrease on CAPS, Loss of Diagnosis: CAPS < 45 and does not meet DSM-IV diagnostic criteria; Total Remission: current CAPS < 20.

Table 4. Outcome on CAPS scores using Group as Unit of Analysis *(n* = 19)

CAPS	*M*	*SD*	95% CI
Pre	70.8	11.3	65.3 to 76.3
Post	47.8***	20.0	38.2 to 57.4
3-month	46.4	14.6	39.4 to 53.5
6-month	47.0	20.4	37.1 to 56.8

Note. ***$p < .001$. CAPS = Clinician Administered PTSD Scale; *M* = Mean; *SD* = Standard Deviation; CI = 95% Confidence Interval.

Table 5. PCL Means (and Standard Deviations) for Treatment Blocks within 16-week Protocol

	Pre	Post			Position (1^{st}, 2^{nd}, 3^{rd})		
	M (SD)	*M (SD)*	Delta		*M* Delta	*M* Delta	*M* Delta
Treatment	[95% CI]	[95% CI]	*M (SD)*	*ES*	Trt 1^{st}	Trt 2^{nd}	Trt 3^{rd}
Cognitive	53.5 (11.7)	49.1 (12.7)	4.4 (10.2)**	0.43	5.2	2.5	6.2
(*n* = 45)	[49.9 to 57.0]	[45.3 to 52.9]					
Exposure	53.6 (12.9)	45.0 (15.1)	8.6 (10.8)***	0.80	12.0	3.5	10.8
(*n* = 44)	[49.7 to 57.5]	[40.4 to 49.6]					
Skills	51.8 (12.7)	47.9 (12.8)	3.9 (8.5) **	0.46	4.7	1.9	4.6
(*n* = 44)	[47.9 to 55.6]	[44.0 to 51.7]					

Note. $^{**}p < .01$, $^{***}p < .001$. PCL = PTSD Symptom Checklist; *M* = Mean; *SD* = Standard Deviation; CI = 95% Confidence Interval; *M* Delta = Mean Change; *ES* = Effect Size(Cohen's *d*); *M* Delta Trt 1^{st} = Mean Change, treatment first position; *M* Delta Trt 2^{nd} = Mean Change, treatment second position; *M* Delta Trt 3^{rd} = Mean Change, treatment third position.

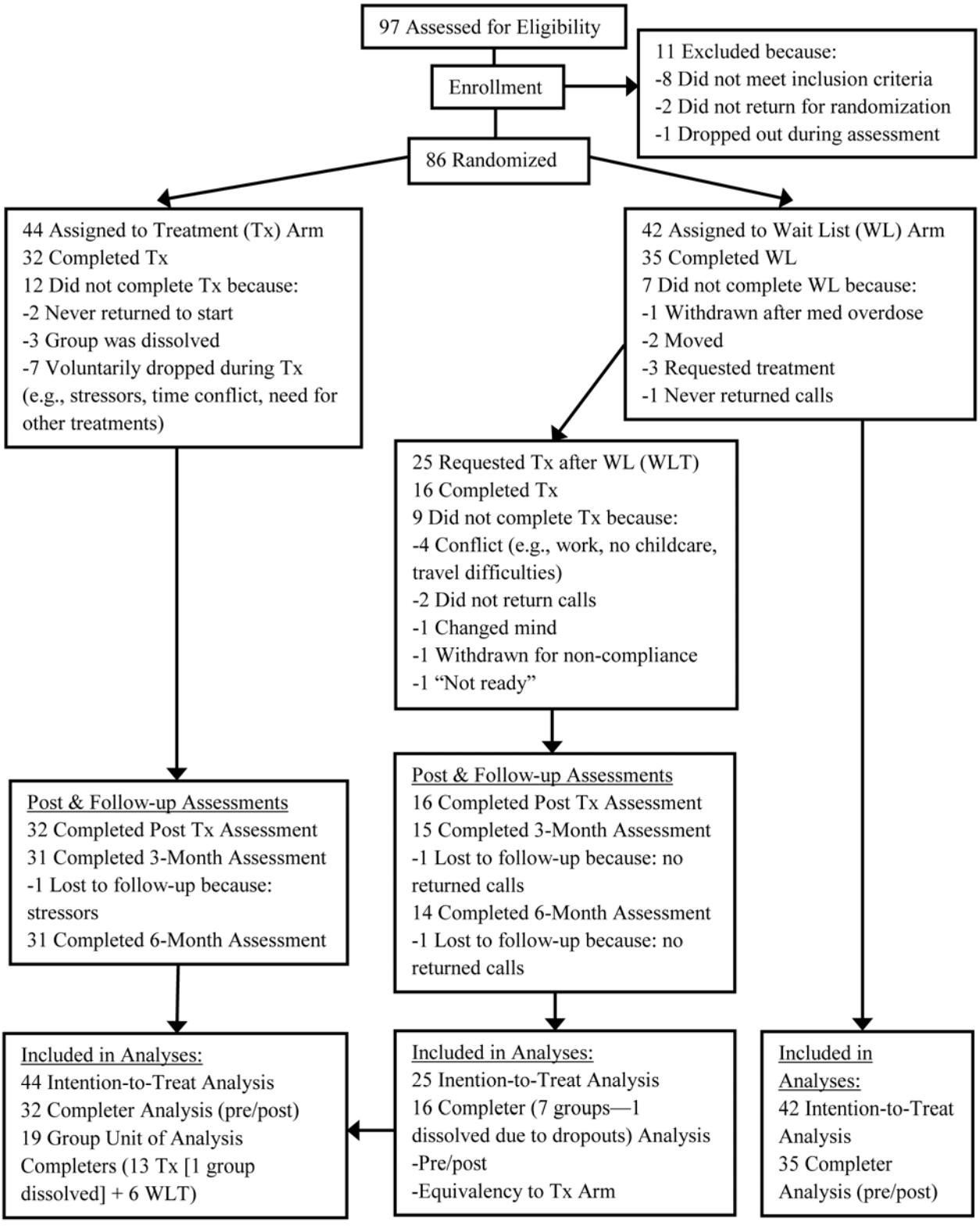

Figure 1. Flow of Participants Through the Trial.

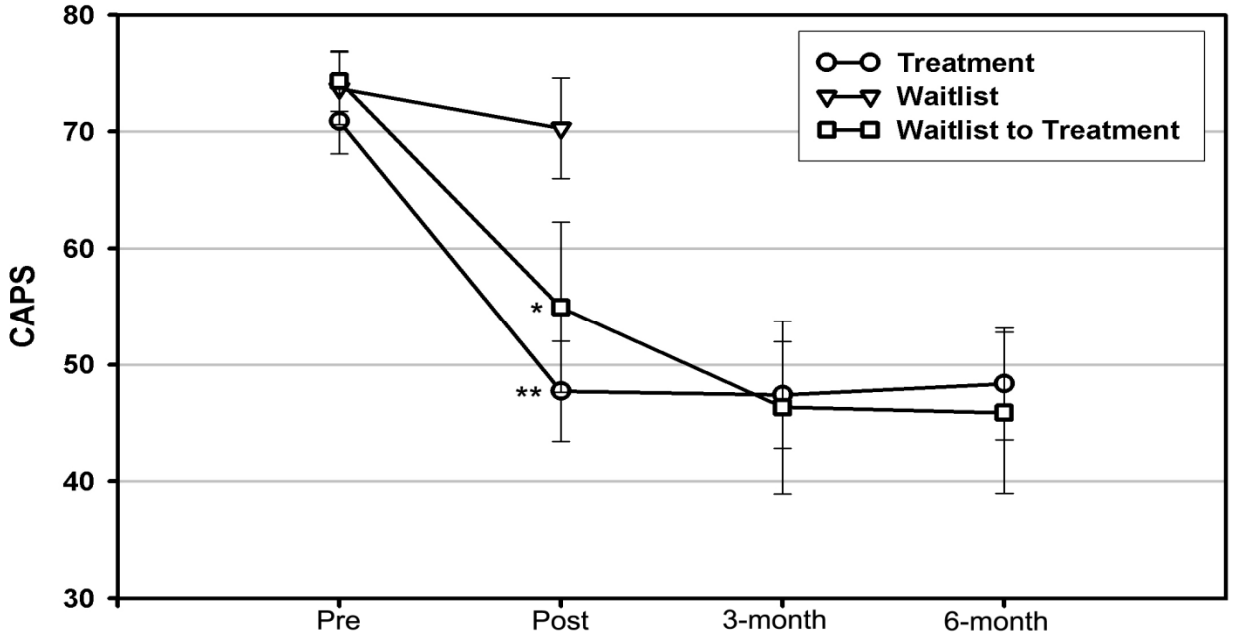

Figure 2a. RM-ANOVA in Intention-To-Treat sample for CAPS scores in three conditions across time. *$p < .01$, **$p < .001$. Error bars represent standard errors. RM-ANOVA = Repeated Measures Analysis of Variance.

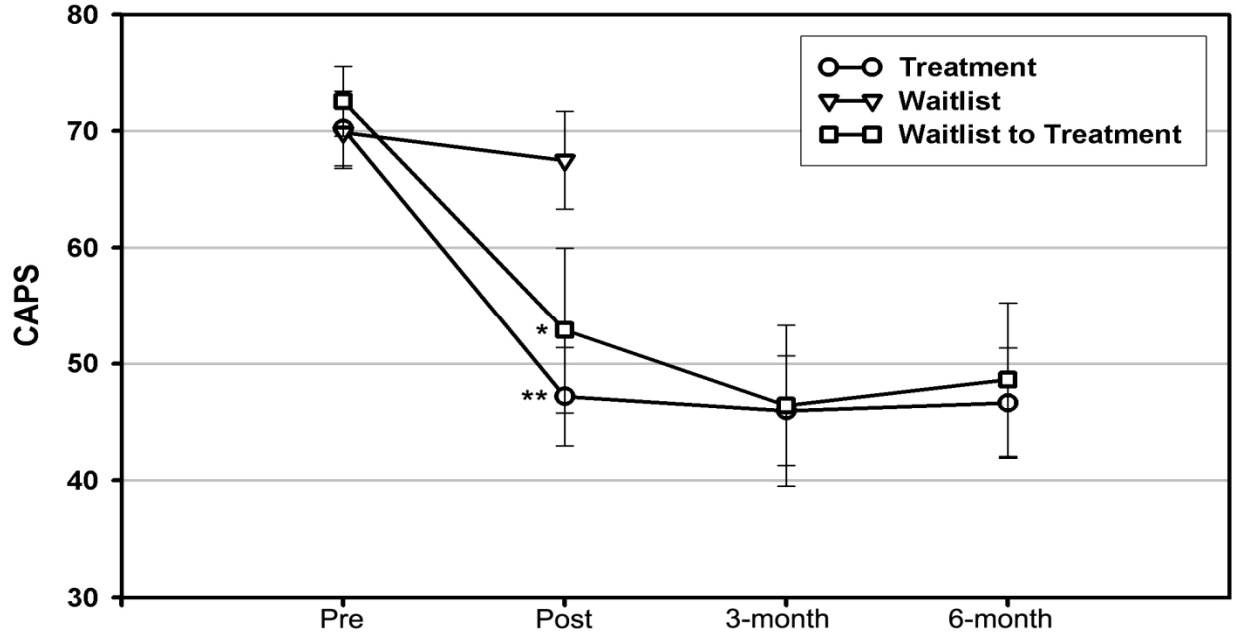

Figure 2b. RM-ANOVA in completer sample for CAPS scores in three conditions across time. *$p < .01$, **$p < .001$. Error bars represent standard errors. RM-ANOVA = Repeated Measures Analysis of Variance.

2. Neuropsychological Differences Manuscript.

Executive Dysfunction Impacts Verbal Learning and Memory in Female Veterans with Post Traumatic Stress Disorder

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Abstract (192)

Neurocognitive problems are common with posttraumatic stress disorder (PTSD) and are important to understand because of their association with PTSD treatment success and its potential neural correlates. This is the first neurocognitive study of female U.S. veterans with posttraumatic stress disorder (PTSD). We examine their neurocognitive profile and assess whether learning deficits, common in PTSD, are attributable to executive dysfunction. 56 female veterans with PTSD and 53 females without PTSD were evaluated for psychiatric and neurocognitive status (estimated IQ, processing speed, executive functions, and verbal learning and retention). The PTSD group had a lower estimated IQ and performed more poorly on all neurocognitive domains, except verbal retention, even when a subset of the 2 groups were matched on IQ and demographics. Only executive functioning for the PTSD group uniquely accounted for significant variance ($p = .008$) in verbal learning over and above IQ, processing speed, depression and PTSD severity. Female veterans with PTSD have a similar neurocognitive profile as male veterans, and executive functioning is a unique predictor of verbal learning weaknesses in PTSD, consistent with the current emphasis in PTSD on executive dysfunction, its prefrontal correlates, and its potential therapeutic implications.

Introduction

PTSD is a growing health crisis in U.S. veterans due to conflicts in Iraq and Afghanistan. Beyond the psychological symptoms that characterize the disorder, cognitive symptoms are common. Neurocognitive problems in PTSD (Vasterling & Brailey, 2005) have been attributed to neurobiological changes associated with the trauma (Southwick et al., 2010), pre-trauma vulnerabilities (Gilbertson et al., 2006), or both. Regardless of their etiology, these neuropsychological characteristics are important to understand as they have been associated with PTSD treatment outcome (Wild & Gur, 2008; Walter, Palmieri, & Gunstad, 2010) and may have implications for the neurobiological substrates of PTSD. In addition, such cognitive weaknesses may support the utilization of therapeutic techniques like attention modification training, which has been shown to improve generalized anxiety (Amir et al., 2009).

Verbal learning and memory is the most commonly identified cognitive problem with PTSD (Vasterling et al., 2002; Brewin, Kleiner, Vasterling, & Field, 2007), but the underlying mechanism of this problem is unclear. One promising explanation has focused on the influence of executive dysfunction, which is consistent with the finding that poor encoding of new information is most prominent, with little evidence of rapid forgetting (Brewin et al., 2007; Vasterling et al., 2002). For example, male veterans with PTSD demonstrated impaired inhibition on a memory test, while there was no evidence of impaired retention of information initially learned (Vasterling et al., 1998). More recent studies have also reported weaknesses in response inhibition (Leskin & White, 2007; Swick, Honzel, Larsen, Ashley, & Justus, 2012) as well as other aspects of executive functioning including set switching (Stein, Kennedy, & Twamley, 2002; Leskin et al., 2007; Gilbertson et al., 2006) and working memory (Jenkins,

Langlais, Delis, & Cohen, 2000; Vasterling et al., 2002). However, no study has assessed if executive dysfunction accounts for poor verbal learning, which is one aim of this study.

Our second aim is to enhance our understanding of neurocognitive weaknesses in female veterans with PTSD. Although PTSD has been studied in men and women, and prevalence rates in civilians is higher in females than males (12.3% vs. 3.6%) (Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995), the neurocognitive impact of trauma on women veterans is poorly understood. Moreover, the incidence of PTSD in female veterans is expected to increase, given their increase in combat responsibilities and the higher incidence of sexual trauma in women in the military (Street, Vogt, & Dutra, 2009).

However, there is no published study of the neurocognitive features of PTSD in female veterans. Most studies that have examined the neurocognitive sequelae of PTSD have relied largely on men with combat-related trauma, which raises concerns about their applicability to female veterans with PTSD. This is particularly important because there are neurobiological differences between men and women that could lead to different neurocognitive profiles (Andreano & Cahill, 2009), though the small number of neurocognitive studies in female civilians have identified problems similar to men (Stein et al., 2002; Jenkins, Langlais, Delis, & Cohen, 1998; Jenkins et al., 2000). The minimal number of neurocognitive studies in females with PTSD is emphasized by a meta-analysis of memory in PTSD (Brewin et al., 2007) that included 27 studies, but only 3 examined women alone (N=52) and none studied female veterans alone. This contrasts with the 12 studies that examined only men (N=356), 10 of which assessed only male veterans (N=314). These findings suggest there is a vital need to examine the neurocognitive profiles of female veterans with PTSD.

Therefore, the major aims of this study were to determine a) if memory and learning problems commonly found in veterans with PTSD are best explained by weaknesses in executive functioning more than other cognitive domains and b) for the first time to examine the neurocognitive sequelae of PTSD in an all-veteran group of women, which we predicted would be similar to previous studies in male veterans with PTSD that show lower, but still normal general intelligence (Gilbertson et al., 2006) and poorer performance in all neurocognitive domains except verbal retention.

Methods

Participants

All participants were female. The PTSD group (N = 56) was comprised of research-referred veterans who served during the Iraq and Afghanistan conflicts. Exclusions from the PTSD group included lifetime or current diagnoses of bipolar or psychotic disorder (n = 1), self-reported learning disability (n = 6), or neurologic diagnoses (n = 0), except for mild traumatic brain injury (mTBI) . The control group (N = 53) was comprised of healthy non-veterans (n = 36) and OIF/OEF veterans without PTSD (n = 17) recruited from the community. Potential controls were excluded if they reported current or previous history of psychiatric (n = 21) or neurologic (n = 10) diagnoses (including mTBI), substance abuse (n = 3), sexual trauma (n = 19), and learning disability (n = 6). The veteran and non-veteran controls were pooled to form a single control group, as they did not demonstrate any significant demographic (p > .705) or IQ (veteran controls: M = 109.4, SD = 11.1; non-veteran controls: M = 104.8, SD = 11.0; p = .163) differences.

Procedures

All PTSD-group participants were enrolled in a research study on the effects of group psychotherapy. They completed clinical and diagnostic interviews, self-report questionnaires, and a neuropsychological battery, before beginning the treatment phase of the study. The control group was screened by telephone, and then completed the same battery of questionnaires and neuropsychological measures as the PTSD group. All participants provided written informed consent, and were compensated for participation. This study was approved by the Institutional Review Board of the New Mexico VA Healthcare System.

Psychological Measures

All participants in the PTSD group completed the Clinician-Administered PTSD Scale [CAPS (Blake et al., 1995)] to verify the diagnosis of PTSD (all scored above the standard PTSD diagnostic cutoff of 50) and the Structured Clinical Interview of Diagnosis [SCID (First, Spitzer, Gibbon, & Williams, 2002)] to assess for co-morbid psychiatric disorders. Both groups were assessed for self-reported PTSD symptoms [PCL; PTSD Checklist (Weathers, Litz, Herman, Huska, & Keane, 1993)], trauma exposure [LEC; Life Events Checklist (Gray, Litz, Hsu, & Lombardo, 2004)], depression [BDI; Beck Depression (Beck, 1987)], and alcohol use [AUDIT; Alcohol Use Disorders Identification Test (Allen, Litten, Fertig, & Babor, 1997)]. Mild TBI was assessed with a modified version of a self-report measure (Fortier et al., 2013), which was based on a change in neurologic status at the time of the worst mild TBI (Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine, 1993).

Neuropsychological Domains

The neuropsychological assessment examined several domains using published tests with demonstrated reliability and validity. Raw scores for all primary measures were transformed to

z-scores based on published age-corrected norms. The z-scores from individual measures within each domain were averaged to obtain a domain score, and when necessary, these z-scores were modified so that positive z-scores reflected better performance. The following domains were assessed:

1. Effort was assessed with the Test of Memory and Malingering [TOMM (Tombaugh, 1997)]; participants were excluded if they scored below 45 on Trial 1 (Hilsabeck, Gordon, Hietpas-Wilson, & Zartman, 2011). One participant from each group was excluded.

2. Estimated General Intelligence was examined with the Wechsler Test of Adult Reading [WTAR (PsychCorp, 2001)].

3. Learning and Memory was assessed with the California Verbal Learning Test-II [CVLT-II, (Delis, Kramer, Kaplan, & Ober, 2000)]. *i. Verbal Learning:* A composite measures used in previous PTSD studies (Vasterling et al., 1998; Gilbertson et al., 2006) was calculated and includes: List A Total Recall, List B Recall, Short Delay Free and Cued Recall, Long Delay Free and Cued Recall, Across-Trial Recall Consistency, Percent Recency Recall, Semantic Clustering, Recognition Hits, and percent change in recall between Short Delay Free Recall and Trial 5 Recall. *ii. Retention* used the published contrast z-score comparing Long Delay Free Recall and Trial 5 Recall.

4. Processing Speed was examined with the Processing Speed Index of the Wechsler Adult Intelligence Scale-IV (Wechsler, 2008).

5. Executive Functioning was comprised of two components combined into a single composite by averaging the z-score composites for each. *Working memory* included the average scaled score for Digit Span Backward, Digit Span Sequencing, and Arithmetic from the WAIS-IV. *Inhibition/Switching* was calculated from four subtests of the Delis-Kaplan Executive Function

System [DKEFS (Delis, Kaplan, & Kramer, 2001)], including Trails 4 (alpha-numeric sequencing), Color-Word Inhibition (naming the color of the print when the word and print were incongruent), Color-Word Switching (shifting on cue from reading the incongruent color word or naming the color of the print), and Category Switching (switching between rapidly generating words in two semantic categories).

Results

The PTSD and control groups did not differ demographically or in alcohol use (See Table 1). The PTSD group reported significantly more different types of trauma (only 3 control participants reported no trauma events), a greater number of PTSD symptoms, and greater depression. While the PTSD group's estimated IQ was within the average range, it was significantly lower than the estimated IQ of the control group.

Primary Analyses

A MANOVA was conducted to assess for overall group differences across the neuropsychological domains (see Figure 1A). The overall model was significant (F (4, 104) = 6.53, $p < .001$, $\eta^2 = .201$) with a large effect size (Cohen, 1988). Significant group differences were observed with medium to large effect sizes for all domains except verbal retention (p = .852, $\eta^2 = .000$) with medium effect sizes for processing speed (F (1, 107) = 10.47, $p = .002$, η^2 = .089) and verbal learning and memory (F (1, 107) = 14.74, $p < .001$, $\eta^2 = .121$) and a large effect size for executive function (F (1, 107) = 18.57, $p < .001$, $\eta^2 = .148$); the PTSD group performed worse on both components of executive functioning [working memory (F (1,107) = 20.64, $p <$ .001, $\eta^2 = .162$), PTSD Mean (SE) = -0.24 (0.08), Control Mean (SE) = 0.35 (0.10) and inhibition/switching [F (1, 107) = 8.62, $p = .004$, $\eta^2 = .075$); PTSD Mean (SE) = 0.18 (0.08), Control Mean (SE) = 0.50 (0.08)].

Next, due to group differences in estimated IQ, we individually matched participants in each group on estimated IQ, age, and years of education. The resulting sample of 42 matched pairs did not significantly differ on IQ (p =.909), age (p = .759), or years of education (p = .542), and the overall MANOVA was significant (F (4,79) = 4.95, p = .002, η^2 = .200) with the same pattern of findings as reported for the entire sample who were not matched on estimated IQ; significant group differences were found for all cognitive domains [processing speed [F (1,82) = 8.76, p = .004, η^2 = .097), executive function (F (1,82) = 12.07, p = .001, η^2 = .128), and verbal learning (F (1,82) = 8.87, p = .004, η^2 = .098]), except verbal retention (F (1,82) = 0.49, p = .49, η^2 = .006) (see Figure 1 B).

Hierarchical regression was conducted with all subjects to examine predictors of memory performance, with sequential entry of the following variables: group, estimated IQ, processing speed, executive composite and group x executive composite. These analyses demonstrated a significant interaction between group and executive functioning when predicting variance in verbal learning and memory (β = .326, ΔR^2 = .053, p = .005), over and above the variance accounted for by all covariates. We therefore examined these relationships separately within each group. Executive functioning explained a significant amount of variance (β = .224, ΔR^2 = .048, p = .008) in verbal learning over and above estimated IQ and information processing speed for the PTSD group only (see Table 2). This relationship was not demonstrated within the normal control group (overall ANOVA and individual standardized coefficients all p > .05).

Supplementary Analyses: Depression, Mild TBI, and PTSD Severity

We conducted a supplementary hierarchical regression in order to assess the potential moderating role of depression in explaining the relationship between verbal learning and executive functioning. Using only the PTSD group, the following variables were entered as

separate steps into the regression: depression scores (BDI), estimated IQ, processing speed, and executive functioning, as predictors of verbal learning. The first step of the model was not significant, indicating that depression alone did not account for a significant amount of the variance in the PTSD group's verbal learning (2.7%, $R = .165$, $p = .226$). Examination of the fourth step of the model demonstrated that inclusion of depression did not affect the overall model, as executive functioning continued to explain a significant amount of variance ($\beta = .343$, $\Delta R^2 = .071$, $p = .016$) in verbal learning over and above depression, estimated IQ and information processing speed.

Another hierarchical regression was conducted to assess the potential moderating role of PTSD severity in explaining the relationship between verbal learning and executive functioning. The analysis was identical to that above except CAPS total was used instead of BDI. The first step of the model was not significant, indicating that PTSD severity alone did not account for a significant amount of the variance in the PTSD group's verbal learning ($\Delta R^2 = .00$, $p = .926$). Examination of the fourth step of the model demonstrated that inclusion of the CAPS did not affect the overall model, as executive functioning continued to explain a significant amount of variance ($\beta = .314$, $\Delta R^2 = = .06$, $p = .029$) in verbal learning over and above CAPS, estimated IQ and information processing speed.

We separated the PTSD group into those who did (N=32) and did not (N=23) self-report a mild TBI to be sure that this factor did not significantly influence our results. No significant ($p < .05$) group differences were observed for any of the demographic (η^2 effect sizes were all small, ranging from .018 to .041) or most psychological variables (e.g., self-report of depression or current alcohol use; η^2 effect sizes were small, ranging from .001 to .036). The mTBI positive group had a higher CAPS score than the mTBI negative group (TBI+ Mean (*SD*) = 78.91

(17.99); TBI- Mean (SD) = 67.0 (17.66); F (1,53) = 5.91, p = .019, η^2 = .106). No group differences were present for the neurocognitive variables, as reflected by a non-significant overall model (F (5,49) = 0.26, p = .93, η^2 = .026; η^2 effect sizes for individual domains ranged from .000 to .010).

We then examined relationships between neurocognitive functioning and PTSD symptom type and severity (within the PTSD group only). Correlations (one-tailed) examined the relationship between PTSD symptom severity using the CAPS and different cognitive domain. There was only one significant correlation between re-experiencing symptoms and processing speed (p = .049). See Table 3.

Discussion

The Impact of Executive Functioning on Verbal Learning and Memory.

As predicted, verbal learning problems, which are commonly reported with PTSD (Brewin et al., 2007), were uniquely associated with executive dysfunction over and above general intelligence, processing speed and depression in the PTSD group, but not in the control group. This relationship had been hypothesized in PTSD, but it has never been directly examined, and it is important in order to better understand the underlying cognitive mechanisms for poorer learning in PTSD. The association of executive functioning and learning has support from studies in healthy individuals and patients with frontal lobe damage (Shimamura, 2008), though our data do not support this relationship in our control group. Our results suggest that the presence versus absence of PTSD, as opposed to severity of PTSD, is the variable that accounts for the relationship between verbal memory and executive functioning within our sample. Entering CAPS total score into the model did not account for any unique variance in this relationship and did not change the effect demonstrated. This negative finding suggests two possibilities. This

relationship may be present before trauma in the PTSD sample reflecting pre-trauma vulnerability, and/or when PTSD severity is above a certain threshold (all of our PTSD sample had CAPS > 50) of severity, or both.

It is well accepted that learning and memory are not unidimensional, and PTSD is associated primarily with impairment in initial learning and retrieval of new information rather than rapid forgetting of information that was initially learned (Vasterling et al., 2002; Stein et al., 2002), consistent with our finding of intact retention. In addition, initial learning is dependent on the ability to maintain multiple pieces of information in working memory, to organize new information in order to facilitate a greater depth of encoding, and to filter and/or inhibit intrusive responses and retrieve correct responses (Shimamura, 2008), all of which are different aspects of executive functioning. Historically, memory deficits in PTSD were emphasized, but a more recent review (Aupperle, Melrose, Stein, & Paulus, 2012b) of neurocognitive problems with PTSD focusing on executive functioning is representative of more current thinking. Our findings suggest that this is an appropriate emphasis since the learning and memory problems seen in our PTSD group were uniquely related to executive dysfunction. This more general impact of executive problems also is consistent with the interest in exploring the neural substrates of executive functioning in PTSD and their implications for treatment. For example, one model (Aupperle et al., 2012b) suggests that weaknesses in executive functions may influence the development and maintenance of PTSD by leading to maladaptive coping styles, such as avoidance. Specifically, impaired ability to inhibit emotional responses to emotionally salient stimuli, trauma memories, or both may lead to avoidance. In this framework therapeutic strategies that enhance executive functions with the goal of inhibiting PTSD symptoms of re-experiencing and arousal to salient, but distracting, internal and external stimuli would be

predicted to be most effective. Attention modification training, which has been shown to improve general anxiety symptoms (Amir et al., 2009), is one such therapeutic option (Aupperle et al., 2012b).

Neurocognitive Weaknesses in Female Veterans with PTSD.

Our results also show that the pattern of neurocognitive weaknesses in female veterans with PTSD is similar to previously published data in male veterans with PTSD and is characterized by poorer but still average general intelligence and poorer verbal learning, executive functions (both working memory and inhibition/switching), and processing speed, but intact verbal retention (See (Vasterling et al., 2005) for review). This pattern of findings did not change after identifying subgroups of PTSD and control participants who were matched for estimated IQ, similar to previous studies. The results are also unlikely to be explained by mild TBI, as we showed comparable cognitive performance across individuals with PTSD who did and did not report a history of mild TBI.

These findings are consistent with other neurocognitive studies in men and women with PTSD which report poorer verbal learning as well as weaker processing speed (Samuelson et al., 2006; Aupperle et al., 2012a) and executive functions including set switching, response inhibition, or attention/working memory (Gilbertson et al., 2006; Swick et al., 2012; Jenkins et al., 2000; Leskin et al., 2007; Vasterling et al., 2002; Parslow & Jorm, 2007; Stein et al., 2002). Studies that have shown no neurocognitive deficits in PTSD have been based largely on non-clinical samples, and in the case of the Vietnam Experience Study data, participants were examined many years after trauma (Crowell, Kieffer, Siders, & Vanderploeg, 2002) though their negative findings may also be due to explicit control of confounding factors, such as psychiatric comorbidities.

While most studies that examine patients with more severe PTSD identify significant neurocognitive deficits, there is some variability in the findings, with, for example, impairment on some but not other tests of executive functioning. This inter-test variability in impairment within studies may be related to the psychometric characteristics of the measures being used. This is illustrated by a recent study in a student population that reported significant deficits in response inhibition using an experimental test (Leskin et al., 2007). The current study has the advantage of combining several standardized clinical neuropsychological measures with good psychometric properties. Using these measures, we have shown that PTSD is associated with relative weaknesses in learning, information processing speed, and executive functioning, which adds to the relatively limited literature in females with PTSD (Stein et al., 2002; Jenkins et al., 2000; Jenkins et al., 1998), especially female veterans because to our knowledge there are no previous studies of neurocognitive profiles in female veterans.

Our findings show that executive functions comprised of working memory and response inhibition and information processing speed were relative weaknesses for this female PTSD group. Although none of these measures are 'pure' indicators of their label, there is evidence that working memory and response inhibition, in particular, are dependent on lateral and medial prefrontal regions to some extent(Aron, Fletcher, Bullmore, Sahakian, & Robbins, 2003). Interestingly, greater activation in the dorsolateral prefrontal cortex has also been associated with better inhibition of unwanted memories in healthy adults (Anderson et al., 2004), which is a potentially important coping mechanism for PTSD. While most structural imaging studies in PTSD have examined the hippocampus and found evidence of decreased volume, one meta-analysis also identified "abnormalities in multiple frontolimbic structures," most notably the amygdala and anterior cingulate cortex (Karl et al., 2006). Several studies have also reported

decreased volume of lateral prefrontal regions (Geuze et al., 2008) in PTSD, and one (Fennema-Notestine, Stein, Kennedy, Archibald, & Jernigan, 2002) reported decreased lateral prefrontal volume with no decrease in hippocampal volume. Of course, the fact that all neurocognitive domains except verbal retention examined were weaker in PTSD argues against a strictly focal neural substrate for PTSD.

Relationship between Neurocognitive Weaknesses and Symptom Severity.

The lack of significant correlation between neurocognitive functioning and PTSD symptom severity was unexpected. We had predicted that poorer executive functions, in particular, would be associated with PTSD severity. However, the only significant relationship was between poorer processing speed and greater re-experiencing symptoms, but this finding must be interpreted cautiously given the number of 1-tailed correlations performed. While some studies have identified such relationships, the details of the relationships have not been entirely consistent. These variable findings are likely related to differences in the PTSD samples, and the neuropsychological and PTSD severity measures used. One previous study of female non-veterans with PTSD due to rape reported no significant relationships between cognition and PTSD severity (Stein et al., 2002), and another (Leskin et al., 2007) reported in a group of undergraduates that greater response inhibition deficits were associated with significantly greater severity of re-experiencing, arousal, and avoidance (r = .35 to .43) only in their female participants. This is inconsistent with our findings since our entire sample was female. However, because all of our study participants were seeking treatment for PTSD and had severe PTSD, this difference in the sample characteristics may explain varying findings. Two studies (Vasterling et al., 1998; Swick et al., 2012) in male veterans also found poorer inhibition was significantly associated with greater re-experiencing, arousal and avoidance. Clearly the relationship between

PTSD severity and neurocognitive function has not been consistently demonstrated suggesting that we have not yet identified the critical moderating variables that impact on this multifactorial relationship.

Limitations

This study has a number of limitations. First, our PTSD group was composed of veterans with significant combat and/or sexual trauma exposure and psychiatric comorbidities while our control group of veterans and non-veterans had less exposure to trauma, and no self-reported psychiatric diagnoses or symptoms of depression. While veteran status does not appear to be critical as our veteran and non-veteran control groups demonstrated no statistically significant demographic or IQ differences, we cannot exclude the possibility that greater trauma exposure in the PTSD group may help to explain the neurocognitive differences across groups. However, our analyses demonstrated that both PTSD severity and self-reported symptoms of depression did not account for the association between executive functions and learning. Unfortunately, the SCID and CAPS were not administered to the control group, which opens the possibility that this group had psychiatric diagnoses that were not identified. However, that is unlikely given their self-report of no psychiatric diagnoses and their low scores on the Beck Depression Inventory. In addition, if such diagnoses were identified in the control group, they would more likely decrease group differences. Second, our PTSD and control groups demonstrated group differences on estimated premorbid intelligence, consistent with many prior studies (Vasterling et al., 1998; Gilbertson et al., 2006). However, our results remained unchanged when using smaller groups matched on this important variable, thus although this remains a limitation to our primary analyses, this does not account for the pattern of results obtained. Finally, the presence of mild TBI in the PTSD group and not in the control group also limits the interpretation of our primary

analyses, but upon further investigation does not appear to be a critical explanation of our results based on our finding that there were no significant cognitive differences between PTSD patients with and without mTBI. Nevertheless, replication of the link between executive functions and verbal learning and memory deficits with PTSD using a control group of veterans with equivalent trauma exposure, history of mild TBI and comparable psychiatric comorbidities would solidify these findings.

Conclusions: These findings, based upon the first study of PTSD in female veterans, suggest that the pattern of neuropsychological findings consistently found in studies of male veterans generalize well to an all female veteran sample. However, the relationship between neurocognitive variables and symptom severity is less consistent. We also found that executive functions explain a significant amount of variance in verbal learning in our PTSD group, but not in healthy controls. This finding, coupled with the fact that our PTSD group did not demonstrate poorer retention of newly learned information, is consistent with evidence that prefrontal abnormalities are significant in PTSD and contribute to memory performance. From a clinical standpoint such executive difficulties, especially those affecting inhibition, may influence the ability to block retrieval of unwanted memories in PTSD (Anderson et al., 2004), which is the major characteristic of re-experiencing symptoms in PTSD. In addition, because attention modification programs are beneficial in the treatment of general anxiety disorders (AMIR 2009b), such focused treatment may be an effective therapeutic strategy for PTSD. Further, focusing cognitive rehabilitation efforts on executive functioning may positively impact memory functioning in PTSD, one of the most common cognitive problems reported and objectively documented.

Reference List

Allen, J. P., Litten, R. Z., Fertig, J. B., & Babor, T. (1997). A Review of Research on the Alcohol Use Disorders Identification Test (AUDIT). *Alcoholism: Clinical and Experimental Research, 21,* 613-619.

Amir, N., Beard, C., Taylor, C. T., Klumpp, H., Elias, J., Burns, M. et al. (2009). Attention training in individuals with generalized social phobia: A randomized controlled trial. *Journal of Consulting and Clinical Psychology, 77,* 961-973.

Anderson, M. C., Ochsner, K. N., Kuhl, B., Cooper, J., Robertson, E., Gabrieli, S. W. et al. (2004). Neural systems underlying the suppression of unwanted memories. *Science, 303,* 232-235.

Andreano, J. M. & Cahill, L. (2009). Sex influences on the neurobiology of learning and memory. *Learning & Memory, 16,* 248-266.

Aron, A. R., Fletcher, P. C., Bullmore, E. T., Sahakian, B. J., & Robbins, T. W. (2003). Stop-signal inhibition disrupted by damage to right inferior frontal gyrus in humans. *Nature Neuroscience, 6,* 115-116.

Aupperle, R. L., Allard, C. B., Grimes, E. M., Simmons, A., Flagan, T., Behrooznia, M. et al. (2012a). Dorsolateral Prefrontal Cortex Activation During Emotional Anticipation and Neuropsychological Performance in Posttraumatic Stress Disorder. *Archives of General Psychiatry, 69,* 360-371.

Aupperle, R. L., Melrose, A. J., Stein, M. B., & Paulus, M. P. (2012b). Executive function and PTSD: Disengaging from trauma. *Neuropharmacology, 62,* 686-694.

Beck, A. T. (1987). *Beck Depression Inventory*. San Antonio, TX: The Psychological Corporation.

Blake, D. D., Weathers, F. W., Nagy, L. M., Kaloupek, D. G., Gusman, F. D., Charney, D. S. et al. (1995). The development of a Clinician-Administered PTSD Scale. *Journal Of Traumatic Stress, 8,* 75-90.

Brewin, C. R., Kleiner, J. S., Vasterling, J. J., & Field, A. P. (2007). Memory for emotionally neutral information in posttraumatic stress disorder: A meta-analytic investigation. *Journal of Abnormal Psychology, 116,* 448-463.

Cohen, J. (1988). *Statistical Power analysis for the behavioral sciences*. (2nd edition ed.) Hillsdale, NJ: Jacob Cohen Publishers.

Crowell, T. A., Kieffer, K. M., Siders, C. A., & Vanderploeg, R. D. (2002). Neuropsychological Findings in Combat-Related Posttraumatic Stress Disorder. *Clinical Neuropsychologist, 16,* 310.

Delis, D. C., Kaplan, E., & Kramer, J. H. (2001). *Delis-Kaplan Executive Function System: Examiner's Manual.* San Antonio: The Psychological Corporation.

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (2000). *CVLT-II Manual*. San Antonio: The Psychological Corporation.

Fennema-Notestine, C., Stein, M. B., Kennedy, C. M., Archibald, S. L., & Jernigan, T. L. (2002). Brain morphometry in female victims of intimate partner violence with and without posttraumatic stress disorder. *Biol Psychiatry, 52,* 1089-1101.

First, M. B., Spitzer, R. L., Gibbon, M., & Williams, J. (2002). *Structured Clinical Interview for DSM-IV-TR Axis I Disorders, Research Version, Patient Edition With Psychotic Screen*. New York: Biometrics Research, New York State Psychiatric Institute.

Fortier, C. B. P., Amick, M. M. P., Grande, L. P., McGlynn, S. P., Kenna, A. P., Morra, L. B. et al. (2013). The Boston Assessment of Traumatic Brain Injury-Lifetime (BAT-L)

Semistructured Interview: Evidence of Research Utility and Validity. [Article]. *Journal of Head Trauma Rehabilitation*.

Geuze, E., Westenberg, H. G., Heinecke, A., de Kloet, C. S., Goebel, R., & Vermetten, E. (2008). Thinner prefrontal cortex in veterans with posttraumatic stress disorder. *Neuroimage, 41,* 675-681.

Gilbertson, M. W., Paulus, L. A., Williston, S. K., Gurvits, T. V., Lasko, N. B., Pitman, R. K. et al. (2006). Neurocognitive function in monozygotic twins discordant for combat exposure: Relationship to posttraumatic stress disorder. *Journal of Abnormal Psychology, 115,* 484-495.

Gray, M. J., Litz, B. T., Hsu, J. L., & Lombardo, T. W. (2004). Psychometric Properties of the Life Events Checklist. *Assessment, 11,* 330-341.

Hilsabeck, R. C., Gordon, S. N., Hietpas-Wilson, T., & Zartman, A. L. (2011). Use of Trial 1 of the Test of Memory Malingering (TOMM) as a screening measure of effort: suggested discontinuation rules. *Clin.Neuropsychol., 25,* 1228-1238.

Jenkins, M. A., Langlais, P. J., Delis, D. A., & Cohen, R. A. (2000). Attentional dysfunction associated with posttraumatic stress disorder among rape survivors. *Clin.Neuropsychol, 14,* 7-12.

Jenkins, M. A., Langlais, P. J., Delis, D., & Cohen, R. (1998). Learning and Memory in Rape Victims With Posttraumatic Stress Disorder. *American Journal of Psychiatry, 155,* 278-279.

Karl, A., Schaefer, M., Malta, L. S., Dorfel, D., Rohleder, N., & Werner, A. (2006). A meta-analysis of structural brain abnormalities in PTSD. *Neuroscience & Biobehavioral Reviews, 30,* 1004-1031.

Kessler, R. C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C. B. (1995). Posttraumatic Stress Disorder in the National Comorbidity Survey. *Archives of General Psychiatry, 52,* 1048-1060.

Leskin, L. P. & White, P. M. (2007). Attentional networks reveal executive function deficits in posttraumatic stress disorder. *Neuropsychology., 21,* 275-284.

Mild Traumatic Brain Injury Committee of the Head Injury Interdisciplinary Special Interest Group of the American Congress of Rehabilitation Medicine (1993). Definition of mild traumatic brain injury. *Journal of Head Trauma Rehabilitation, 8,* 86-87.

Parslow, R. A. & Jorm, A. F. (2007). Pretrauma and posttrauma neurocognitive functioning and PTSD symptoms in a community sample of young adults. *American Journal of Psychiatry, 164,* 509-515.

PsychCorp (2001). *Wechsler Test of Adult Reading Manual*. San Antonio: The Psychological Corporation.

Samuelson, K. W., Neylan, T. C., Metzler, T. J., Lenoci, M., Rothlind, J., Henn-Haase, C. et al. (2006). Neuropsychological functioning in posttraumatic stress disorder and alcohol abuse. *Neuropsychology, 20,* 716-726.

Shimamura, A. P. (2008). A Neurocognitive Approach to Metacognitive Monitoring and Control. In J.Dunlosky & R. Bjork (Eds.), *Handbook of Memory and Metacognition* (pp. 373-390). Mahwah, NJ: Erlbaum Publishers.

Southwick, S., Davis, L., Aikins, D., Rasmusson, A., Barron, J., & Morgan III, C. (2010). Neurobiological Alterations Associated with PTSD. In M.J.Friedman, T. M. Keane, & P. A. Resick (Eds.), *Handbook of PTSD Science and Practice* (Paperback ed., pp. 166-189). New York: The Guilford Press.

Stein, M. B., Kennedy, C. M., & Twamley, E. W. (2002). Neuropsychological function in female victims of intimate partner violence with and without posttraumatic stress disorder. *Biological Psychiatry, 52,* 1079-1088.

Street, A. E., Vogt, D., & Dutra, L. (2009). A new generation of women veterans: Stressors faced by women deployed to Iraq and Afghanistan. *Clinical Psychology Review, 29,* 685-694.

Swick, D., Honzel, N., Larsen, J., Ashley, V., & Justus, T. (2012). Impaired response inhibition in veterans with post-traumatic stress disorder and mild traumatic brain injury. *J Int.Neuropsychol.Soc., 18,* 917-926.

Tombaugh, T. N. (1997). The Test of Memory Malingering (TOMM): Normative data from cognitively intact and cognitively impaired individuals. *Psychological Assessment, 9,* 260-268.

Vasterling, J. & Brailey, K. (2005). Neuropsychological Findings in Adults with PTSD. In J.Vasterling & C. R. Brewin (Eds.), *Neuropsychology of PTSD - Biological, Cognitive, and Clinical Perspectives* (pp. 178-207). New York: The Guilford Press.

Vasterling, J. J., Brailey, K., Constans, J. I., & Sutker, P. B. (1998). Attention and memory dysfunction in posttraumatic stress disorder. *Neuropsychology., 12,* 125-133.

Vasterling, J. J., Duke, L. M., Brailey, K., Constans, J. I., Allain, A. N., & Sutker, P. B. (2002). Attention, learning, and memory performances and intellectual resources in Vietnam veterans: PTSD and no disorder comparisons. *Neuropsychology, 16,* 5-14.

Walter, K. H., Palmieri, P. A., & Gunstad, J. (2010). More than symptom reduction: changes in executive function over the course of PTSD treatment. *J.Trauma Stress., 23,* 292-295.

Weathers, F., Litz, B., Herman, D., Huska, J., & Keane, T. (1993). The PTSD checklist (PCL): Reliability, validity, and diagnostic utility. In San Antonio, TX.

Wechsler, D. (2008). *Wechsler Adult Intelligence Scale—Fourth Edition (WAIS-IV)*. (4 ed.) San Antonio: Pearson.

Wild, J. & Gur, R. C. (2008). Verbal memory and treatment response in post-traumatic stress disorder. *The British Journal of Psychiatry, 193,* 254-255.

Table 1. Group Demographics and Psychiatric Characteristics, Mean (Standard Deviation)

	Healthy Controls	PTSD	Significance	Effect Size
	N = 53	*N* = 56	*p*	η^2
Age	37.1 (11.7)	36.8 (11.5)	.870	.000
Years of Education	15.2 (1.9)	14.7 (1.7)	.137	.021
Estimated IQ	106.3 (11.1)	100.0 (12.9)	.007	.066
Beck Depression	2.8 (3.0)	26.3 (10.1)	<.001	.711
Types of Trauma, #[1]	2.9 (1.5)	7.7 (2.9)	<.001	.528
CAPS[2]	N/A	72.1 (18.5)		
PCL[3]	17.1 (0.4)	59.9 (18.9)	<.001	.723
Alcohol Use Disorder Test	2.0 (1.8)	2.7 (2.6)	.112	.023
Ethnicity, Number (%)			.547*	
White	19 (35.9%)	15 (26.8%)		
Hispanic	20 (37.7%)	26 (46.4%)		
Other	14 (26.4%)	15 (26.8%)		
Mild Head Injury	N/A	26 (46%)		

[1] Life Events Checklist (LEC)
[2] Clinician Administered PTSD Scale (CAPS)
[3] PTSD Symptom Checklist (PCL)
* Based on χ^2

Table 2
Final regression model for PTSD group: executive functioning predicts verbal learning and memory.

	Statistics for predictors		
	β	*T*	*p*
WTAR Standard Score	0.324	2.624*	0.011
Processing Speed	0.134	1.060	0.294
Executive Functioning	0.317	2.279*	0.027

Table 3. Correlations between Domains of Neuropsychological Functioning, and PTSD Symptom Type and Severity in the PTSD Group

	Neuropsyc Average	Processing Speed	Verbal Learning	Response Discrimin	Executive Function	Inhibition	Working Memory
CAPS Total	.059	.159	.013	-.018	-.001	.004	-.004
CAPS Re-experiencing	-.005	.223*	-.081	-.066	.077	.069	.064
CAPS Avoidance	.037	.057	.022	.027	-.104	-.098	-.083
CAPS Arousal	.112	.118	.087	-.016	.245	.066	.030

* $p < .05$

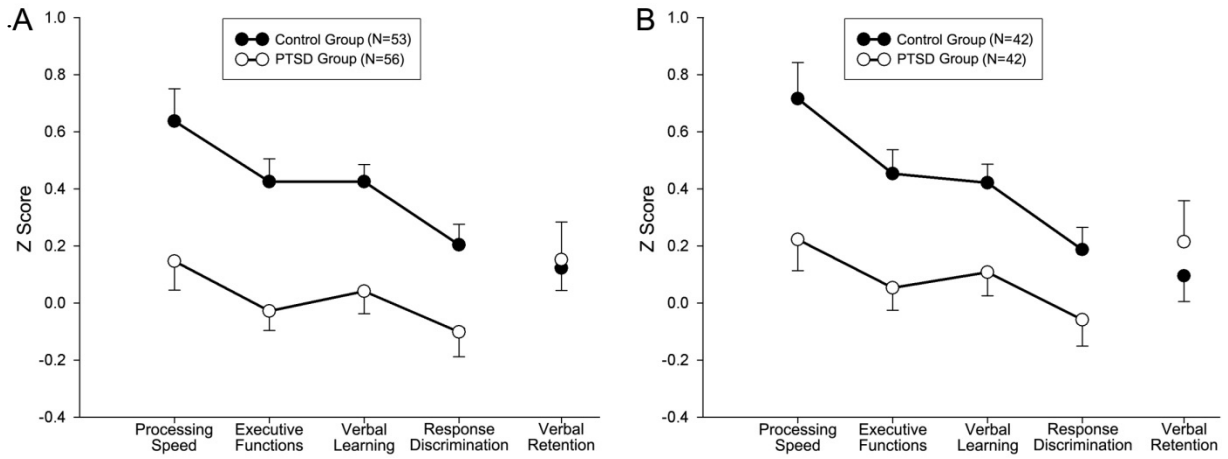

Figure 1. Mean with standard error of measurement (SEM) bars for all neurocognitive domains for A) entire PTSD and Control groups and B) for PTSD and control subgroups matched for estimated IQ.